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FIBROSIS OF THE PANCREAS IN INFANTS AND CHILDREN

AN ILLUSTRATED REVIEW OF CERTAIN CLINICAL FEATURES WITH SPECIAL EMPHASIS ON THE PULMONARY AND CARDIAC ASPECTS

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THERE has been a tendency in descriptions of fibrosis of the pancreas to select certain combinations of manifestations and proclaim corresponding "types" of the disease.[9, 12] Consequently one hears surprise expressed when a patient is encountered who cannot be fitted neatly into one of these abstract types. The many natural variations in symptoms demand a more dynamic concept of this disease. Then the less commonly appearing combinations of symptoms will take their place as understandable variations in a coherent, basic process. All the fluctuations in respiratory symptoms, variations in the feces, and contrasting degrees of nutritional disturbances are the result of different systems being affected simultaneously and continuously but with independently varying intensity.

It is our intention to portray the interplay of certain aspects of the disease as they may appear in different age periods and at various times in the same patient. Much of the evidence supporting this point of view has appeared in previous reports.[6, 14, 16, 18, 22, 26, 28, 29] This is augmented herein by a series of illustrative figures and further clinical descriptions derived from 134 patients whom we have studied. A bibliography of selected papers is appended for reference and as a guide in obtaining a more complete knowledge of the disease.

The name generally employed for this disease, "cystic fibrosis of the pancreas," is misleading because: (1) it focuses attention on one aspect, perhaps the least vital, of the disease, no hint being made of the constant lesion in the lungs although this aspect of the disease appears to be the most important one in determining the clinical course and the fate of the victim; (2) no suggestion of the variability of the symptoms is revealed through the fixed lesion of the pancreas; (3) this terminology has served to overemphasize the nutritional problem and the role of diet in the treatment of the disease. Although the theory of pathogenesis advanced by Farber and Wolbach (generalized alteration in mucous secretions leading to obstruction, dilatation, atrophy, and fibrosis of secreting glands) is an intriguing, unifying concept,[2, 18] it is not sufficiently established to justify adopting the proposed name "mucoviscidosis."[10] Fibrosis

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of the pancreas, the term we employ, at least has the merit of being noncommittal and containing no factual error.

At the outset it must be clear that we are dealing here only with the fully developed disease, fibrosis of the pancreas. By this we mean that other forms of pancreatic insufficiency, such as that due to atresia of the pancreatic duct, are not of concern to us at present.

It is conceivable that all grades of severity of altered secretions might exist, from minimal microscopic changes, which could hardly cause symptoms, up to the more profound and widespread changes that cannot but produce symptoms. Actually we have never encountered any confusion clinically. We have never recognized any minimal or subclinical stages of the disease, primarily because symptoms are not produced until the involvement in the pancreas and lungs has become advanced and widespread. Whenever a patient has been shown to have this disease, even when examined so early that symptoms were very mild, we have found the pancreatic enzymes to be virtually absent from the duodenum and the lungs already clearly abnormal as demonstrated by clinical or roentgenographic examination. Other organs or systems have given no symptoms unless they have been severely affected. It appears to us that there is a wide gap between the minimal findings on microscopic examination discovered in patients dying of some disease other than fibrosis of the pancreas and the unequivocal pathologic changes which are invariably found in those dying with all the clinical manifestations of fibrosis of the pancreas.

There is need for better evidence that the basic pathologic process may appear in all stages of development at any age, before or after birth. All the clinical evidence is for a process appearing just before, at, or shortly after birth with rapid progression to full development with symptoms promptly produced.

MECONIUM ILEUS

Meconium ileus is the least complicated exhibition of the underlying process. As early as 1905 Landsteiner,[1] because of a lesion which he demonstrated in the pancreas, suggested that intestinal obstruction in the newborn infant from inspissated meconium might be dependent on absence of pancreatic secretion. Others found the same alteration in meconium with simple atresia of the pancreatic duct.[20, 21] In the majority of infants with meconium ileus, a lesion indistinguishable from that occurring in infants with fibrosis of the pancreas who never had meconium ileus has been found in the pancreas.[22]

Meconium ileus is a disease of full-term infants. In our experience, premature infants have not been affected. Meconium sufficiently inspissated to obstruct the intestine would seem to be a sign that the pancreatic lesion is so advanced that no appreciable pancreatic secretion reaches the intestine. Only twenty-nine of our 134 patients with fibrosis of the pancreas developed meconium ileus.[33] This would indicate that the lesion develops rapidly near term but may not reach its full extent until after the meconium is passed.

The final link in relating meconium ileus to fibrosis of the pancreas was provided by success in relieving the intestinal obstruction and maintaining survival long enough for the telltale pulmonary lesions to fully develop. Four patients illustrate this sequence of events. One was born with meconium ileus.

The obstruction was relieved by surgery and enteral irrigations with pancreatin. By intensive administration of fluid and other supportive therapy, he survived with an ileostomy. During the ensuing weeks, he developed classical clinical and roentgenologic signs of the pulmonary lesion, and was found to have no trypsin in his duodenal secretions. He is still alive and represents an unmistakable example of true fibrosis of the pancreas of the sort regularly encountered that usually escapes meconium ileus. Two other patients who endured an identical sequence of events for two and six months, respectively, gradually acquired definite clinical signs of the disease (Plate XII). At necropsy all the usual findings in the lungs and pancreas were found to be present in these cases.

The link between meconium ileus and fibrosis of the pancreas is further illustrated by a boy, now 6 years old, who had signs of intestinal obstruction at birth and who fortunately was relieved of obviously inspissated meconium by rectal irrigations with pancreatin solution.[26, Fig. 9] After a brief period of "wheezing" he was free of pulmonary signs but developed grossly fatty stools and was treated for celiac disease for four years without satisfactory response. Then his ravenous appetite and foul stools were correlated with the neonatal history and five examinations of his duodenal secretions over a two-year period revealed no tryptic activity. Furthermore, his lungs now show definite roentgenographic findings such as we have seen in other children with fibrosis of the pancreas who have relatively quiescent chronic pulmonary disease. He also has a chronic sinus infection with *Staphylococcus aureus* which produces extraordinarily viscid mucoid secretions.

Many of the children with fibrosis of the pancreas who did not have intestinal obstruction at birth, may nevertheless have had alterations in the viscosity of their meconium proportional to the degree of pancreatic failure. All gradations of difficulty in passing meconium during the neonatal period may be anticipated in such cases. The subsequent course of patients with inspissated meconium or meconium ileus tends to follow the sequences illustrated by this sample group. However, there is not a clear-cut "type" of patient surviving meconium ileus apart from or different from the group with fibrosis of the pancreas.

All infants suffering from meconium ileus or unusual difficulty in passing meconium ought to be suspected of fibrosis of the pancreas. If relieved of intestinal obstruction, they should have the pancreatic enzymes assayed and observed in the following months with due regard for the possibility of development of the pulmonary lesion. Rarely a child will turn out to have congenital atresia of the pancreatic duct or other pathology of the pancreas without developing pulmonary lesions. Quantitative information as to the composition of meconium in pancreatic insufficiency is lacking. This might be of value in distinguishing inspissation from this cause from variation of normal meconium which might be viscid enough to cause confusing symptoms.

THE PANCREATIC LESION

It may be deduced from the information already given that the clinical evidence strongly suggests (1) that the lesion in the pancreas develops early, just prior to, at, or soon after birth; (2) that it must progress rapidly to loss of function of the exocrine portion of the pancreas; and (3) that once fully de-

veloped, it is irreversible, repair and recovery not occurring; the damage is complete and final. It is well known that clinical symptoms would not be expected unless this were true, for very little normal pancreas would suffice to carry out its usual function in digestion. This has been proved experimentally in animals and by patients who have undergone subtotal pancreatectomy. In one such patient in our experience, the concentration of pancreatic enzymes in the duodenum hardly reflected the loss of approximately nine-tenths of the pancreas, the absorption of nitrogen and fat were unimpaired, and the nutrition was unaffected.

We have found on analysis of our clinical data[33] that, besides the patients with meconium ileus, others with fibrosis of the pancreas develop symptoms of pancreatic insufficiency soon after birth. One-third have abnormal stools from birth. Many fail to gain weight in the first weeks of life in spite of abundant intake of food and inconspicuous pulmonary symptoms. Fully two-thirds show one or another symptom of pancreatic insufficiency by the age of 4 weeks. That no return of pancreatic function occurs, once it is destroyed, has been demonstrated in our patients again and again throughout long periods with repeated duodenal enzyme analyses (over a period of six years in one patient). This evidence for lack of pancreatic enzymes and the irreversibility of the pancreatic lesions has been abundantly verified by clinical observations and metabolic balance studies.[14-17]

It is obvious then that the contribution pancreatic insufficiency makes to the total clinical appearances in this disorder ought to be a constant one. The variability in the features of the disease must be dependent on other factors.

One consideration which might lead to an *apparent* variability in the consequences of complete pancreatic insufficiency is an extraordinary adaptation which the body can make to the lack of pancreatic enzymes. It has been shown that the absorption of both fat and protein frequently can be 60 per cent or more of normal without the aid of pancreatic enzymes.[14-17] This adaptation may take time to develop and the degree of adaptation may be variable so that fluctuations in the efficiency of digestion and in symptoms might be expected to occur. The "plateau" period of failure to gain weight, frequently observed during the first three months of life,[26] may be explicable on such a basis.

A fortunate feature in this disorder is the preservation of a good appetite or the development of a really ravenous one. This leads to excellent or increased intake of food and compensates more or less for the inefficient digestion. If there is no extra burden to carry such as infection or severe pulmonary lesions, normal nutrition is frequently maintained. In fact, patients with this disease who follow their instinct, uninhibited by medical care, and consume large quantities of well-balanced diets, often maintain themselves in excellent nutrition. This led to questioning the value of dietary restrictions and to concentrating attention on the pulmonary process.[26] It is noteworthy that maintenance of good nutrition does not prevent the ultimate appearance of characteristic pulmonary symptoms, often even in a severe form.

The ravenous appetite, inefficient digestion compensated for by increased intake of ordinary foods, and ability to maintain good health for long periods without pancreatic enzymes had been observed in experimental animals before this disease was described.[13] It should be recalled, however, that such animals,

free of pulmonary disease, often exhibited mysterious slumps in their appetite, food intake, and weight gain. It has not been possible to disentangle such a phenomenon in our patients from the other more obvious causes of decline such as those attributable to the pulmonary process.

The clinical evidence of the pancreatic lesion is found in the feces. The most dependable sign is increased bulk and weight of feces. Impairment of digestion cannot but lead to increased fecal excretion. Commonly, mothers and even doctors and nurses state that the feces of a patient with fibrosis of the pancreas appear normal. Ordinarily, what is meant is that the feces are formed, not fatty or foul, and individual specimens are not unduly large. But were the output of feces of an entire day to be seen, or the increased number of formed stools noted, it would be evident that the total fecal excretion is always greater than normal. Although a specimen of the feces may be formed, and not abnormally large, it is much more usual for the feces to be abnormal in appearance. The stools are sometimes unformed but not frequent, which condition can easily be confused with chronic diarrhea. Rarely they are numerous and loose. Initially they do not often appear fatty. Beyond the first year of life they are frequently fatty and pale as well as bulky, mushy, and foul. Sometimes actual drops of fat separate from the feces. During certain periods, according to the diet perhaps, the stools may be frothy and irritating to the buttocks, leading to an erroneous diagnosis of "carbohydrate intolerance." In the same patient any of the various appearances of the feces may predominate from time to time: all are equally "characteristic" none is diagnostic, but all are seen in many forms of chronic intestinal insufficiency. A rare patient consistently passes stools so normal in appearance that only total weight or metabolic balance study reveals the extent of the fecal wastage of undigested food. Ample opportunity for this great variety in the appearance of the feces is allowed by differences in age of the patients, types of diet, fluctuations in absorption, along with the variable burden provided by the pulmonary lesion.

It may be pointed out that the impairment of absorption of fat particularly affects the fat-soluble vitamins. Normal levels of vitamin A in the blood, and presumably also of vitamin D, have always been maintained by simply increasing the oral dose of these fat-soluble vitamins to approximately three times normal amounts. According to the results of recent studies of the absorption of emulsified forms of the fat-soluble vitamins,[23, 24] the selection of a more dependable means of administering these substances to patients with impaired absorption of lipids may be possible. Parenteral injection of fat-soluble vitamins is both unnecessary and unwise. If the impaired absorption is not compensated for by increasing intake, deficiency may occur. In fact, all of the examples of deficiency of vitamin A which we have recognized clinically or pathologically resulted from failure to provide even ordinary amounts of supplementary vitamin A.[6] Rickets has occurred only once in our experience, more because of the retardation in growth, perhaps, than because of deficiency vitamin D has not occurred. Undercalcification of the bones is found almost regularly.

Thus, even the various consequences of the fixed lesion in the pancreas can only be encompassed by a dynamic concept interrelating the insufficiency of external secretion of the pancreas with the other aspects of the disease.

This sort of understanding makes practical management more rational and appropriate. The diet may as well be a well-balanced one given to satisfy the appetite. The usefulness of pancreatin is questionable because of its low or uncertain enzyme potency, expense, and the relatively little improvement effected in absorption. It frequently lessens appetite and undermines this compensatory mechanism. A better enzyme product for substitution therapy would be desirable. The feces are a reliable, but not diagnostic, sign of the disease, requiring close scrutiny for correct evaluation. Little hope can be offered for ultimate elimination of the pathology in the pancreas. Fortunately the course and fate of the patient are determined more by other factors which may be reversible, mild, or more successfully controlled. There is no evidence that the severity of the pulmonary process is in any way directly dependent upon the severity of the pancreatic lesion.

THE PULMONARY LESION

It seems desirable to give a somewhat more extensive consideration to the pulmonary lesion accompanying fibrosis of the pancreas because descriptions in the literature are fragmentary and scattered. A comprehensive picture of the course and significance of the pulmonary process is necessary for accurate diagnosis, proper management, and sound prognosis. Only by a full appreciation of the dynamic interplay between the variable components forming the lesion in the lungs can one understand the wide gamut and smooth gradation of the clinical manifestations.

On pathologic examination[18] of the lungs an unusually viscid mucopurulent secretion is seen exuding from the bronchi. Microscopically the bronchioles are found plugged with a mixture of homogeneous mucus and purulent exudate. There are varying degrees of inflammatory response usually limited to the peribronchial region, occasionally leading to areas of alveolar consolidation, but more commonly to bronchiolectasis or scattered small abscesses. The lung parenchyma is affected primarily with the emphysema and atelectasis which are the inevitable result of bronchiolar obstruction. Interstitial fibrosis is usually not conspicuous. Infection with *Staph. aureus* is regularly present. The type of infection is unique in the infant age period in that the invasiveness characteristic of the *Staph. aureus* is not apparent and the systemic response is very subtle. But, in spite of this indolence, the infection is remarkably persistent. Whether the pathology in the lungs is due to this infection, to elaboration of an unusually thick mucoid secretion by the bronchial glands, or, as seems possible, to a combination of both, cannot be regarded as settled.

Patients who die of meconium ileus, having survived but a day or two, may not show characteristic pathology in the lungs, but all such patients who have lived longer have abnormal lungs (vide supra). Only three patients with fibrosis of the pancreas have been encountered by us who were essentially free of pulmonary complaints. In each case roentgenograms of the lungs revealed minimal peribronchial infiltration and emphysema. Thus it appears that the pulmonary lesion is a regular accompaniment of the pancreatic lesion and has its inception simultaneously with it.

The clinical signs and symptoms are clearly referable to variation in the severity of the different elements in the pathology. A consideration of the accompanying photographs and their legends in the order arranged (Plates I-XII) allows one to pass from an illustration of the simplest pulmonary involvement to increasingly complex and varied manifestations of disease in the chest. This approach provides an array of the clinical phenomena likely to be encountered. A clear conception of the basis of these manifestations may be facilitated by the text which follows.

Clinical signs and symptoms include wheezing, dyspnea, cough, the production of sputum composed of tenacious, mucoid substance or a thick, mucopurulent material, cyanosis sometimes associated with clubbing of fingers and toes, fever, and deformity of the chest. These occur in various combinations to provide the appearances which are seen in the various phases of the disease. During the neonatal period, wheezing or dyspnea may be noted without other symptoms or signs. Three instances of pathology in the lungs without clinical symptoms have already been mentioned. Cough is usually a prominent symptom before 6 months of age and frequently dates from birth. When the disease is progressive, dyspnea increases until cyanosis finally appears, often as early as 2 to 5 months of age. One-fourth of our patients developed cyanosis at some time. At the onset of dyspnea in the infant retraction of the intercostal spaces is common, but if the process continues severe the thoracic cage assumes a barrel shape in later months and years. Sooner or later in the great majority of patients a respiratory infection is contracted, and in its wake there remains a chronic pulmonary infection with *Staph aureus*. Whereas before, occasionally a scanty clear viscid sputum had been observable in the pharynx on coughing, after the infection is established, a viscid, mucopurulent, yellow or green, often copious, sputum is seen or may be expectorated by the older child. The *S. aureus* is so regularly and predominantly the infecting organism that it almost bears the role of a stigma of the disease. At this point, while a slight fever may be present, there usually is none and the systemic reaction is more one of insidious decline in the total physical and nutritional condition of the patient than of an overwhelming reaction.

As these signs and symptoms are described, one might gain the impression there is an ominous march of events toward inevitable doom. Quite to the contrary, the progression may halt at any point and even be reversed to an improved or even symptomless state. In fact, seven of our patients even lost their cyanosis as they improved.

Findings on physical examination are variable, depending on degree of bronchiolar obstruction, character of the exudate, extent of the process, and occurrence of infection. There may be gradual fluctuation in the signs but at times the change from one phase to another is so rapid as to suggest that there may be an element of muscular spasm about the involved bronchioles. Proof of spasm is scanty, but suggestive responses to antispasmodic agents have occasionally been observed. The outstanding findings are those of emphysema: diminished tidal exchange, distant vesicular breath sounds, resonance, and hyperresonance. Atelectasis is not often massive enough to give definite signs such as dullness or bronchial breathing but is usually a roentgenographic or micro-

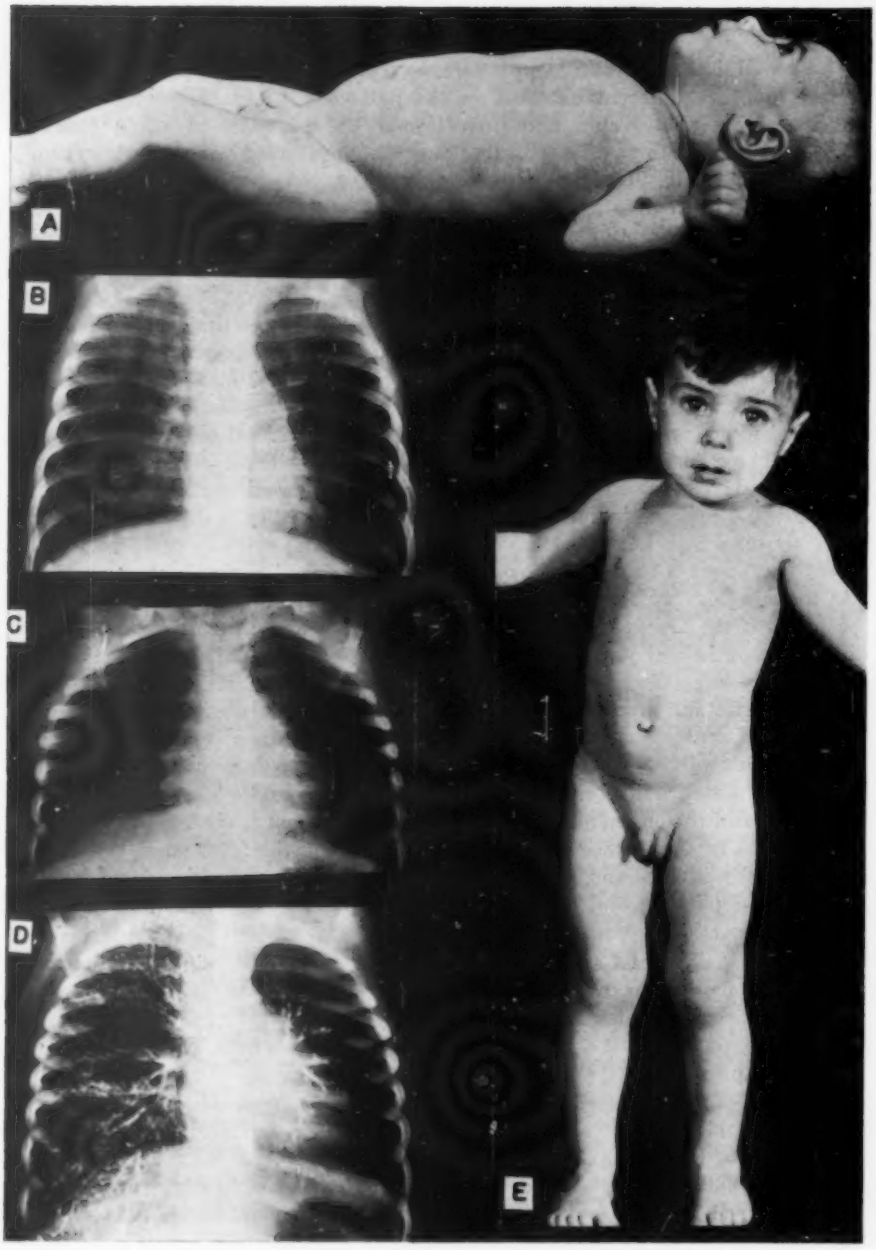

PLATE I.—J. N., *A*, Patient at 6 mnoths. *B*, Lungs at 6 months. *C*, Lungs at 2 years, 2 months. *D*, Bronchogram at 2 years, 2 months. *E*, Patient at 2 years, 2 months.

Fibrosis of the pancreas can exist with but minimal pulmonary complaints. This undoubtedly was due to mild and intermittent bronchiolar obstruction. Possibly there was some element of smooth muscle spasm, but evidence of infection was lacking. Nutritional state was excellent both at 6 months and at 2 years. Roentgenograms show minimal peribronchial infiltration early and moderate emphysema later. Lipiodol bronchograms revealed no bronchiectasis.

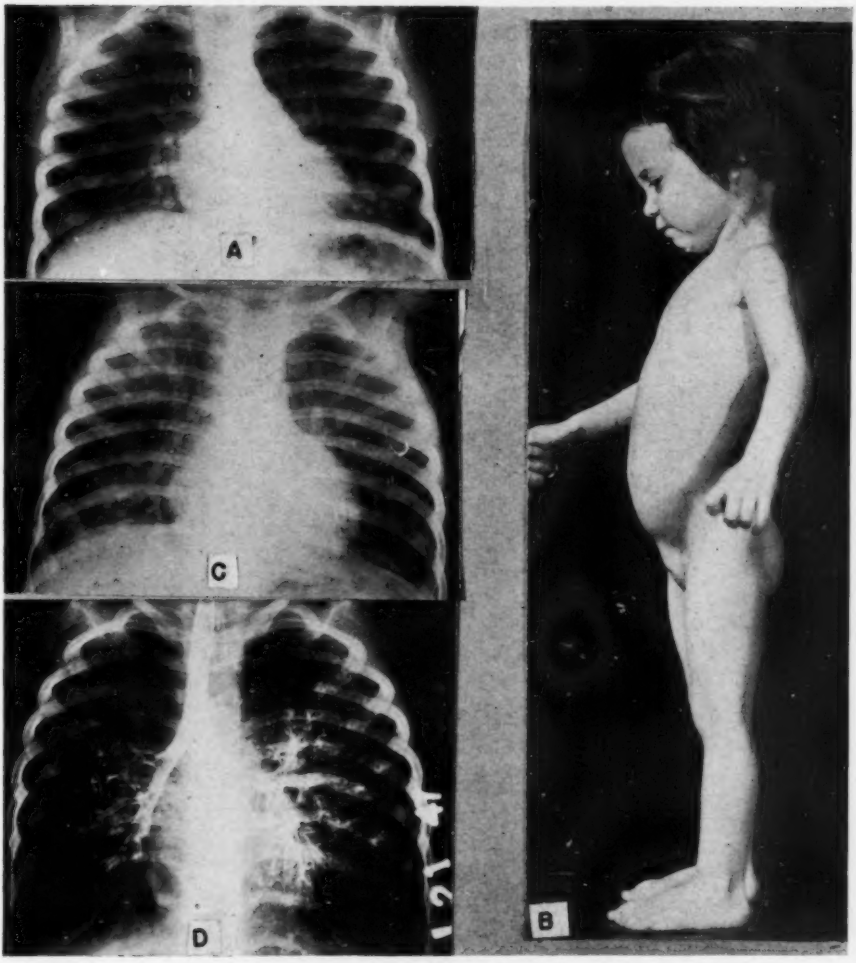

PLATE II.—L. G., *A*, Lungs at 2 years, 8 months. *B*, Patient at 2 years, 8 months old.

Moderate peribronchial infection, when superimposed upon the existing basic pathology of altered secretions, may very early cause a decrease in weight gain and growth. This patient had periods of exacerbation of her pulmonary infection during which weight gain was poor. At these times evidence of parenchymal disease was obvious by physical examination and x-ray. During interim periods weight gain was good and evidence of disease was lacking. This x-ray taken during a quiescent period demonstrates slight emphysema and moderate peribronchial infiltration. At this time minimal clubbing of the fingers was first noted.

C. D., *C*, Lungs at 1 year, 10 months. *D*, Bronchogram at 2 years, 11 months.

Most children with mild pulmonary infections have periods of improvement and periods of increased disease. The child whose chest is shown by roentgenogram above had these periods but retained an area of constant infection in the right lower lobe. This was more apparent on physical examination than by x-ray since râles were always present here.

The early x-ray demonstrates a common concomitant of bronchiolar obstruction; atelectasis. This is almost always patchy in distribution and seems to be at least in part related to the infection which is superimposed upon the latered secretions. Certainly it is related to obstruction of smaller bronchi and bronchioles. This is best shown by the fact that when the infection improves much of the atelectasis disappears. The bronchogram at 2 years, 2 months demonstrates poor filling in the right lower lobe bronchus. Diminution of atelectasis and the appearance of moderately severe emphysema may also be seen.

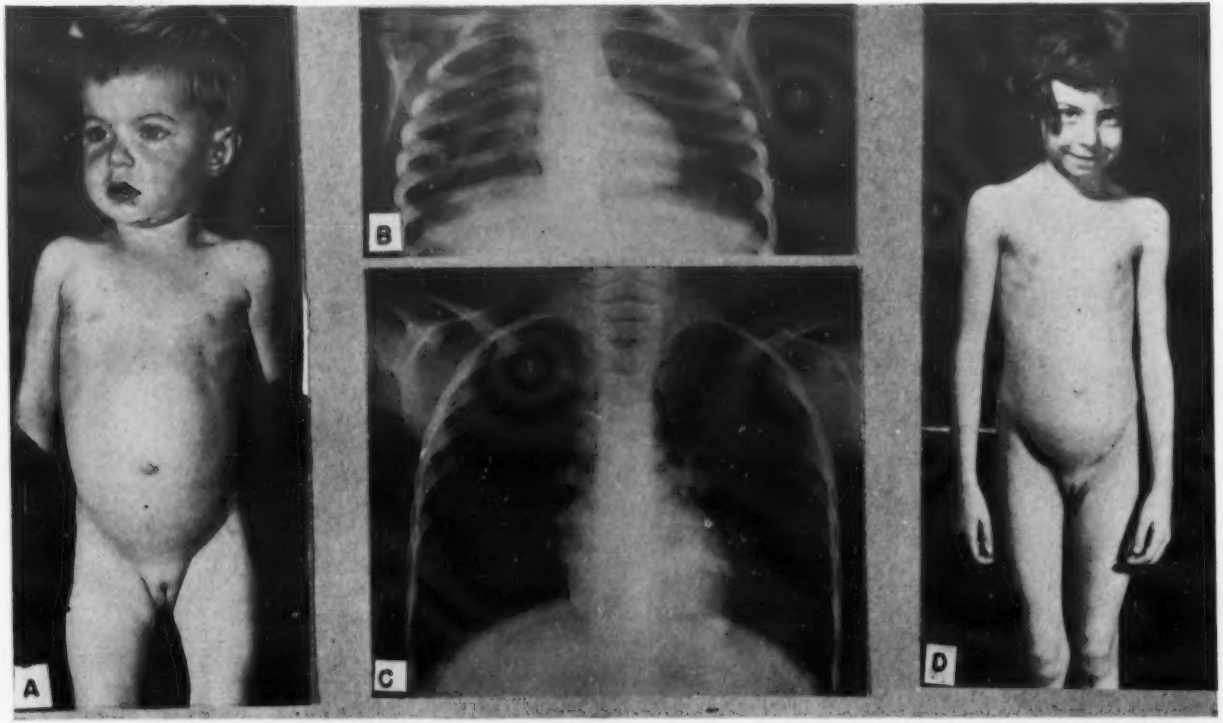

PLATE III.—B. H., *A*, Patient at 1 year, 5 months. *B*, Lungs at 1 year, 5 months. *C*, Lungs at 8 years. *D*, Patient at 8 years.

Sometimes patients who have moderate pulmonary disease in early childhood may survive with little or no therapy and grow remarkably well. Undoubtedly, the basic pulmonary pathology remains, but bronchiolar obstruction is minimal and infection mild.

This child was followed for six and one-half years. Physical examination at 8 years of age revealed no pulmonary abnormalities, but the roentgenogram of the chest showed mild emphysema and minimal peribronchial infiltration.

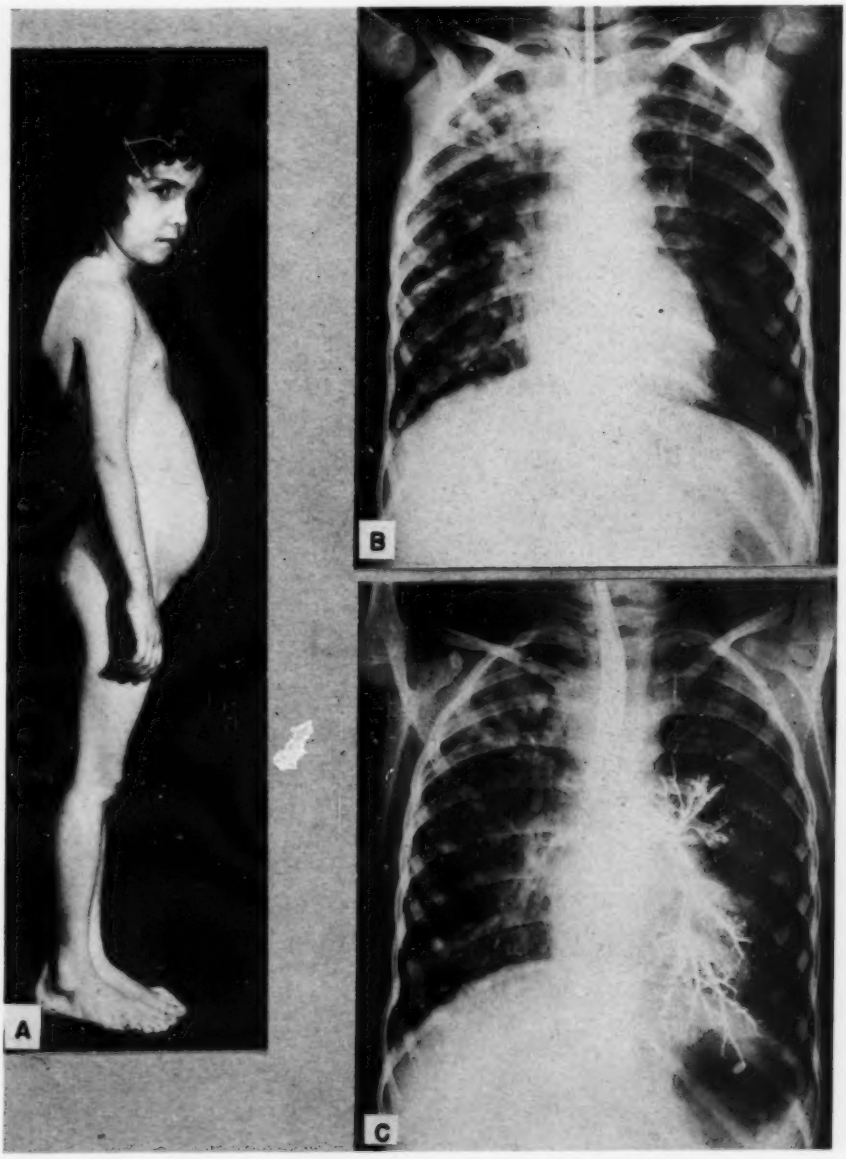

PLATE IV.—J. F., *A*, Patient at 8 years. *B*, Lungs at 7 years, 10 months. *C*, Bronchogram at 7 years, 10 months.

Apparently children can survive long periods with even severe pulmonary disease. This child was first seen at 8 years of age, never having had pulmonary complaints severe enough to demand the attention of a physician. She had obviously severe disease both by x-ray and on physical examination, and clubbing of the fingers was marked. The roentgenogram revealed scattered ateiectasis and emphysema, peribronchial infiltration and patchy pneumonic consolidation. Lipiodol bronchograms showed extensive bronchiectasis, one of the few cases encountered in the group of living children.

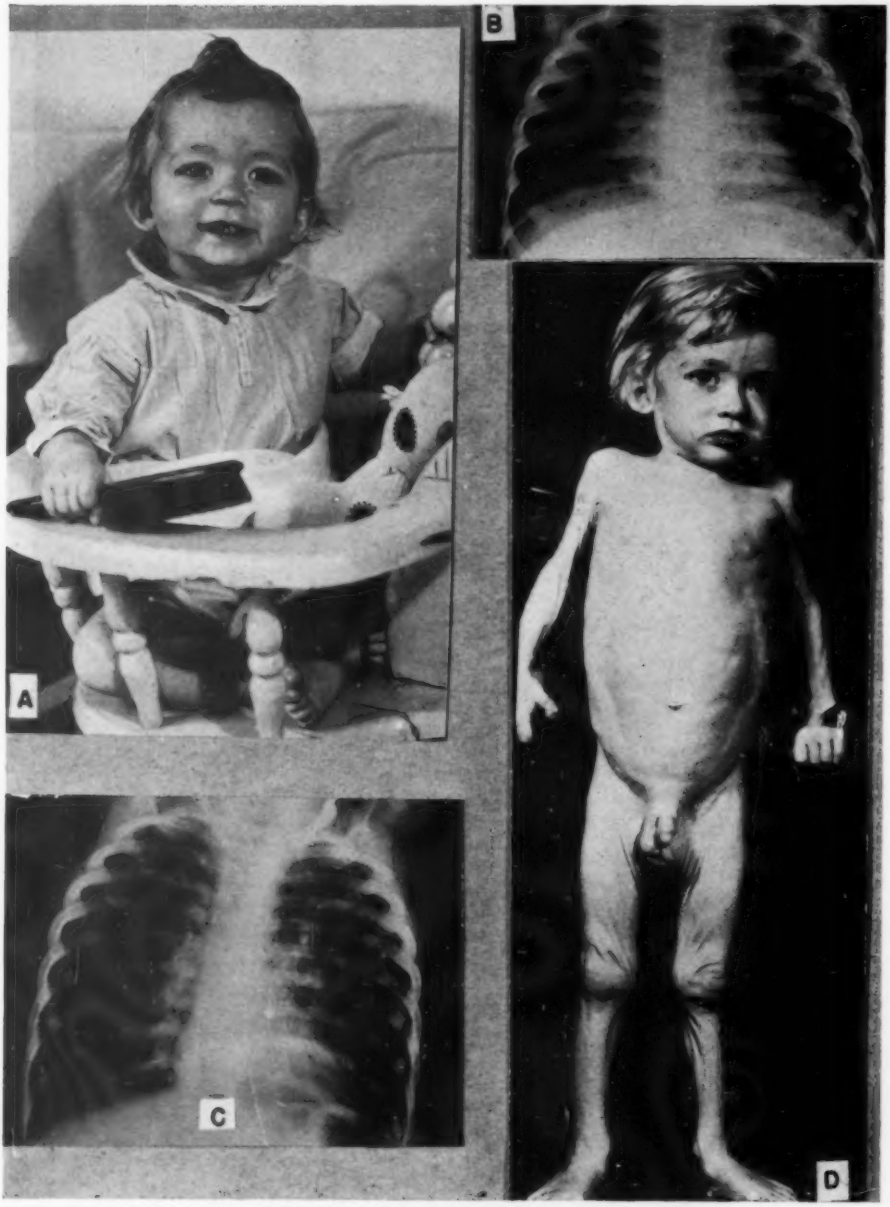

PLATE V.—N. R., *A*, Patient at 1 year, 7 months. *B*, Lungs at 1 year, 2 months. *C*, Lungs at 2 years, 5 months. *D*, Patient at 2 years, 5 months.

If the areas of infection persist, the periods of remission become less frequent and the exacerbations more severe, nutritional state suffers, and the patient becomes more obviously wasted. This child failed steadily and within ten months became marasmic and died. His x-rays show progress of both peribronchial infiltration and emphysema and an increase in the areas of atelectasis and focal pneumonitis.

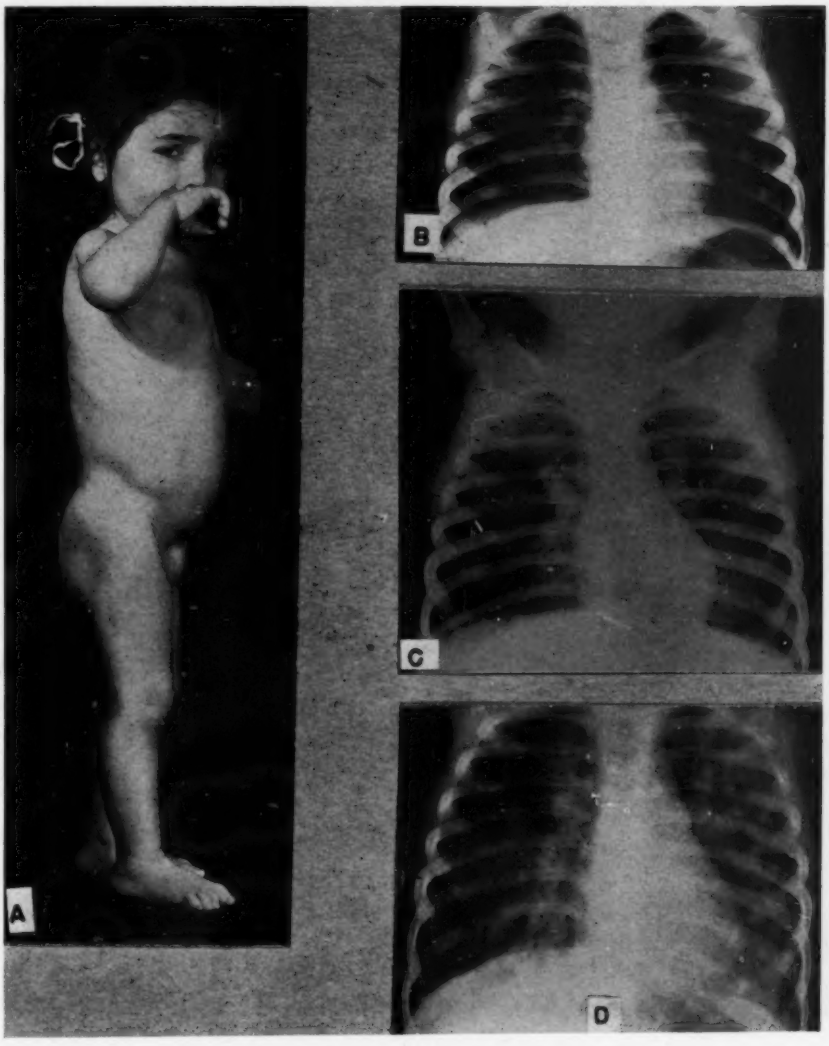

PLATE VI.—M. C., *A*, Patient at 1 year, 10 months. *B*, Lungs at 1 year, 3 months. *C*, Lungs at 1 year, 10 months. *D*, Lungs at 2 years.

Adequate nutrition and a mild pulmonary lesion early in life is no promise of a benign clinical course. This child was robust and active when first seen with what was thought to be a mild right lower lobe pneumonia. The diagnosis of fibrosis of the pancreas was not even suspected. Seven months later she still had adequate subcutaneous tissue but her chest was severely diseased. Peribronchial infiltration, patchy atelectasis and pneumonia, and emphysema were all marked. Within two months she was dead. The roentgenogram taken just before death illustrates the remarkable rapidity with which the pulmonary lesion progressed.

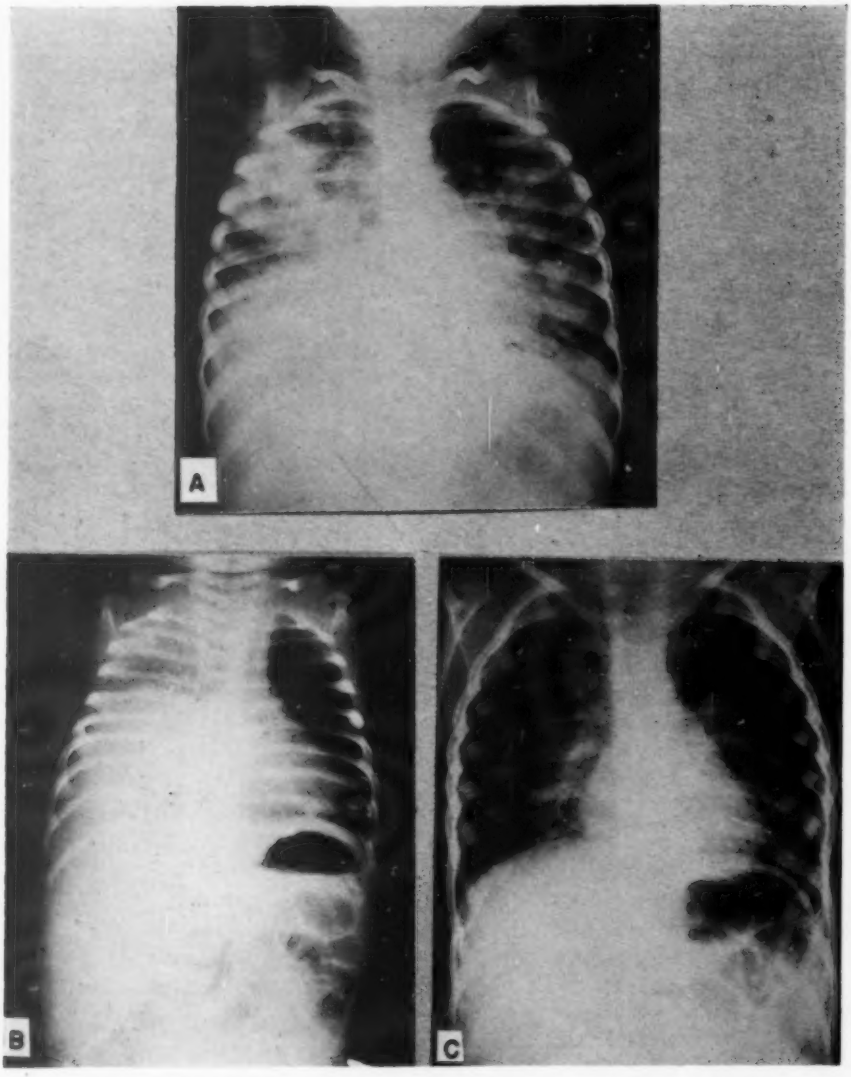

PLATE VII.—D. C., *A*, Lungs at 2 years, 2 months. The pneumonitis at times can reach extraordinary degrees of severity. It is, however, superimposed upon the basic pathology and although this roentgenogram shows extremely severe pneumonia on the right, the left chest shows the expected peribronchial infiltration, patchy atelectasis, and emphysema.

There is a curious host-parasite relationship between the *Staph. aureus* and patients with fibrosis of the pancreas. Only rarely do these children show the expected complications of pulmonary infection with this organism, in spite of the fact that it is almost uniformly present. Septicemia, abscess formation, and empyema are very rare. Two children have been seen with empyema. One of these died (D. M.); *B*, lungs at 3 months. The other survived and two and one-half years later was growing well (M. B.): *C*, lungs at 2 years, 10 months, eighteen months after empyema resolved. His chest roentgenogram is not normal but physical examination is not remarkable.

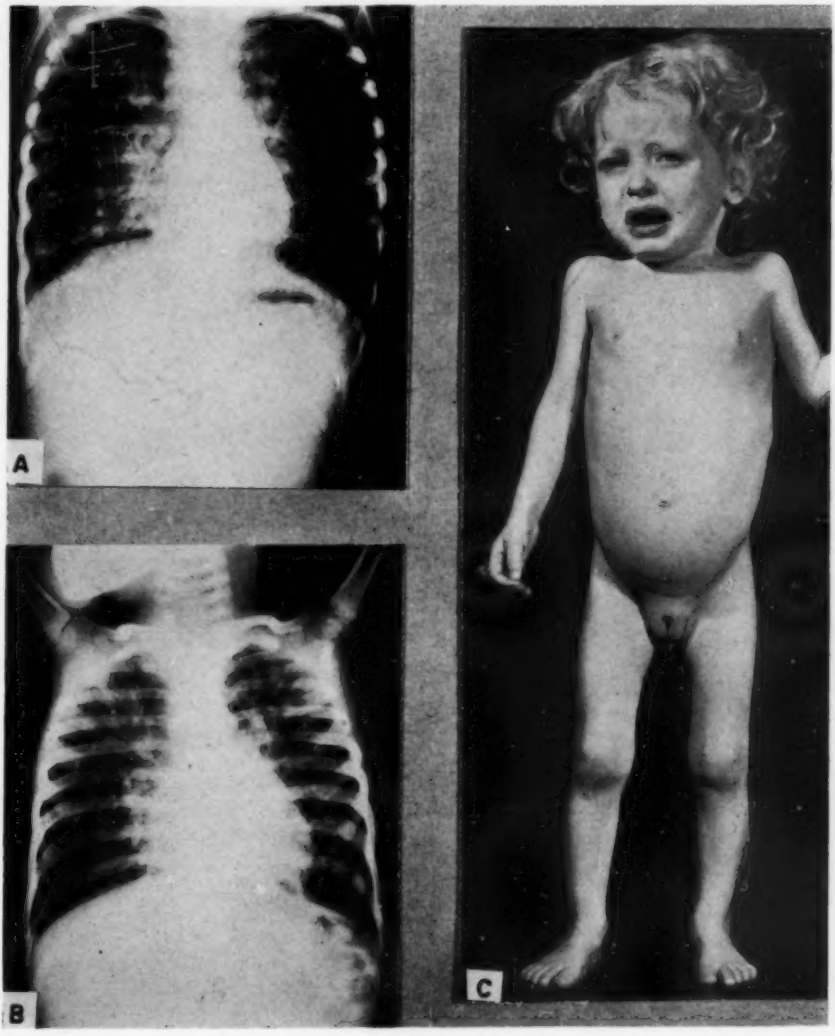

PLATE VIII.—H. P., *A*, Lungs at 2 years, 10 months.

Emphysema, a natural sequel to partial bronchiolar obstruction may be a serious and eventually even fatal complication of the pulmonary lesion in patients with fibrosis of the pancreas. In certain children this is the most conspicuous feature of the clinical pathology. When it becomes severe, it may cause death from anoxia. Infection is usually not clinically very obvious, but clubbing of the fingers and cyanosis are prominent.

M. T., *B*, Lungs at 2 years. *C*, Patient at 1 year, 5 months.

Asphyxia was the most prominent feature of this child's terminal days. The evidence of peribronchiolar infiltration was mild; atelectasis and pneumonitis were minimal but emphysema was extreme. The diaphragm was down to the tenth interspace.

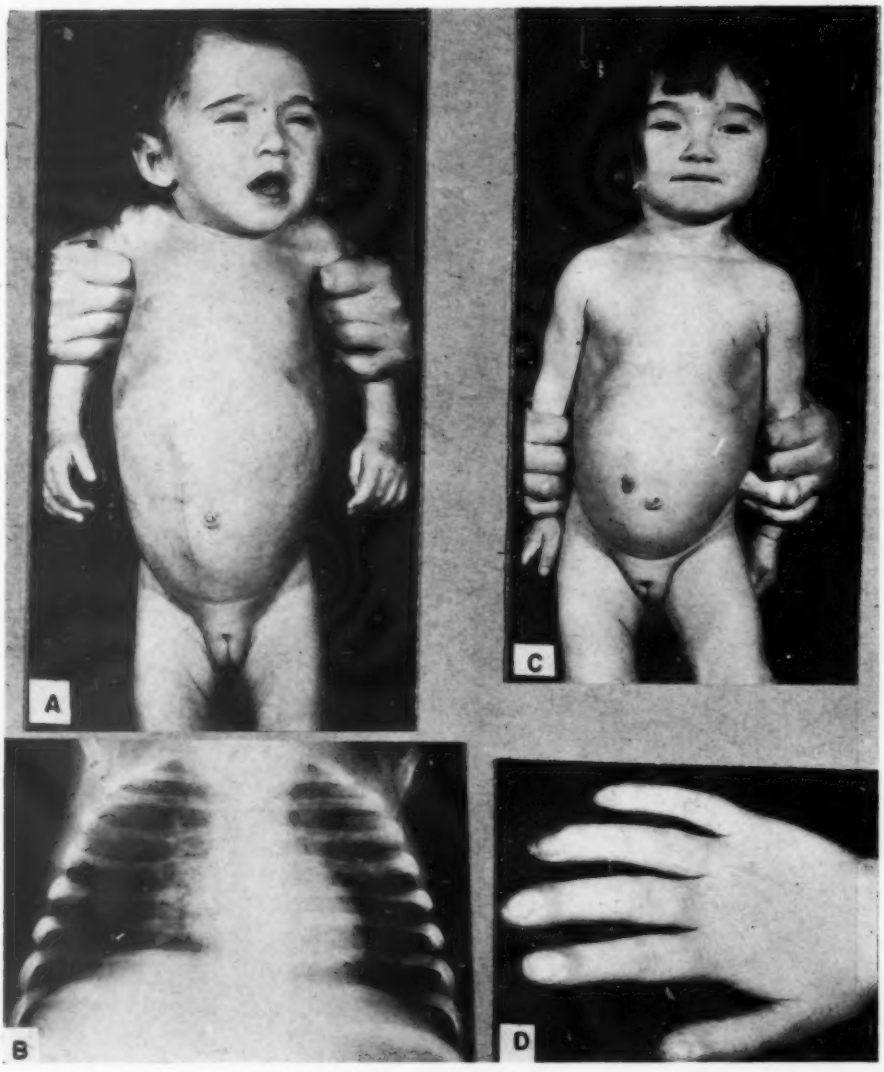

PLATE IX.—E. M., *A*, Patient at 7 months. *B*, Heart and lungs at 6 months. *C*, Patient at 11 months. *D*, Fingers at 3 years, 7 months. *E*, Heart and Lungs at 3 years, 6 months. *F*, Heart and lungs at 3 years 7 months. *G*, Heart and lungs at 4 years, 3 months. *H*, EKG at 3 years, 8 months. *I*, EKG at 3 years, 10 months. *J*, patient at 4 years.

Heart failure may complicate the disease of patients who have suffered a protracted course characterized not only by repeated and severe pulmonary infection but also severe emphysema.

This child had pneumonitis of a mild degree at 7 months followed by an apparent remission until the age of 3½ years. However, her chest then showed marked infiltration as well as emphysema. During the next month her heart enlarged considerably and soon thereafter evidence of heart failure was present. At 4 years of age, she had anasarca, cyanosis, marked clubbing of the fingers. An electrocardiogram showed right axis deviation. Terminally, the heart became huge and progressive right axis deviation was demonstrated by electrocardiogram. The abdominal scar is a result of an appendectomy in infancy.

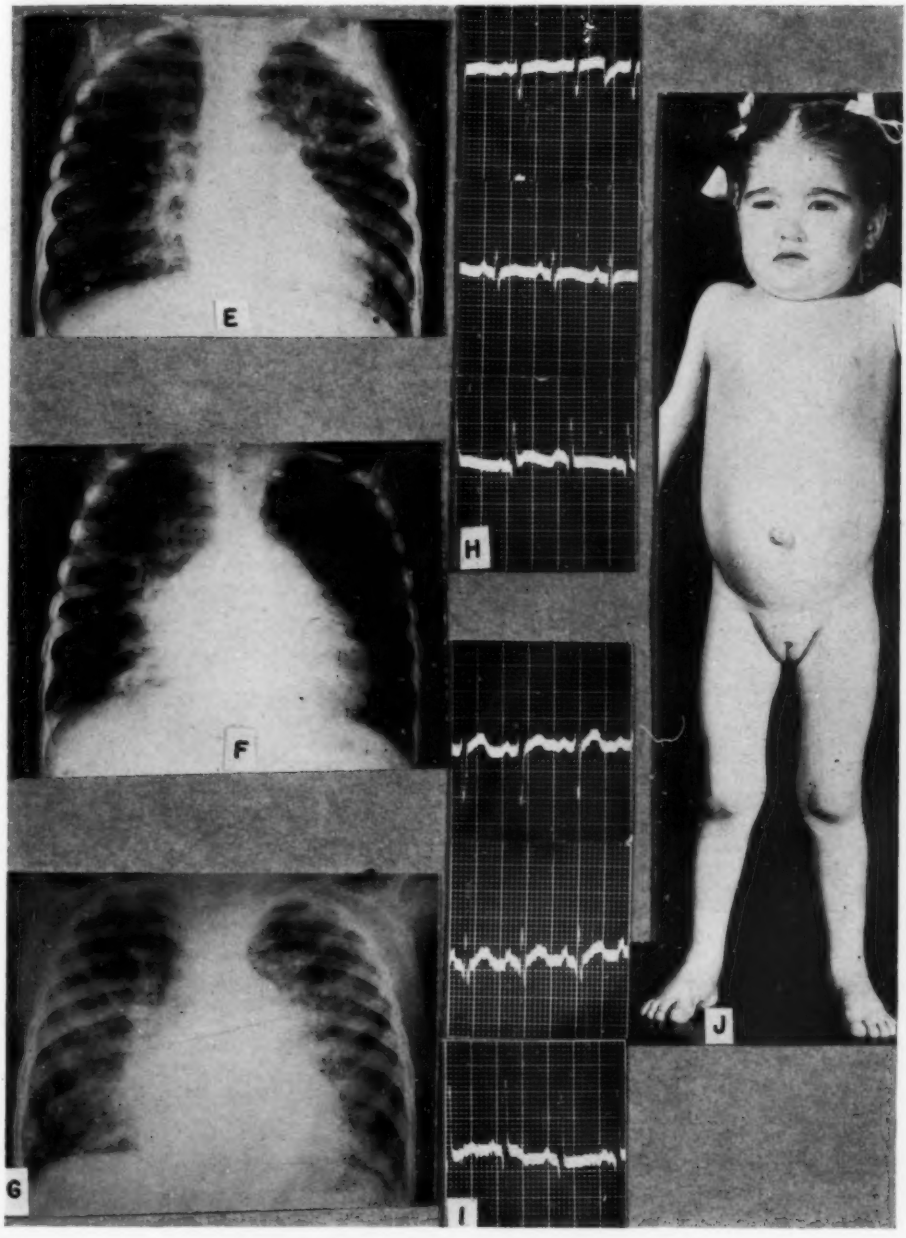

PLATE IX *Cont'd.—For legend see opposite page.*

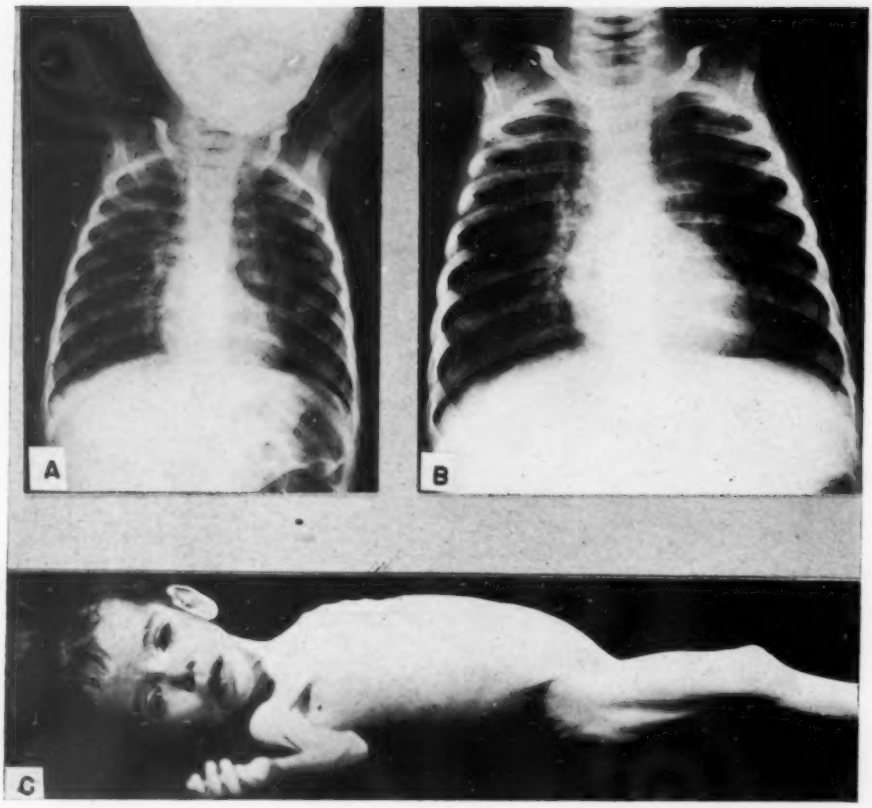

PLATE X.—C. R., *A*, Heart and lungs at 7 months. *B*, Heart and lungs at 14 months. *C*, Patient at 12 months. *D*, Heart and lungs at 19 months. *E*, Heart and lungs at 20 months. *F*, Heart and lungs at 20½ months. *G*, Heart and lungs at 21 months.

Although all patients who developed heart failure eventually died, an occasional patient has had a remission of edema and decrease in heart size for a short period of time.

This child was followed closely for eighteen months. A bronchogram made during infancy was not unusual. Progressive dyspnea as well as permanent cyanosis appeared. At 14 months, the heart seemed proportionally larger than it had seven months previously. At 19 months, the heart had increased still further and edema suddenly appeared. Without digitalis, but while receiving large doses of the B complex of vitamins, her heart decreased in size and the edema disappeared. While receiving the same therapy, her heart suddenly enlarged again and edema returned. From then until the time of death, two weeks later, the edema and heart size both increased. Throughout the period when edema was present, the serum protein was normal.

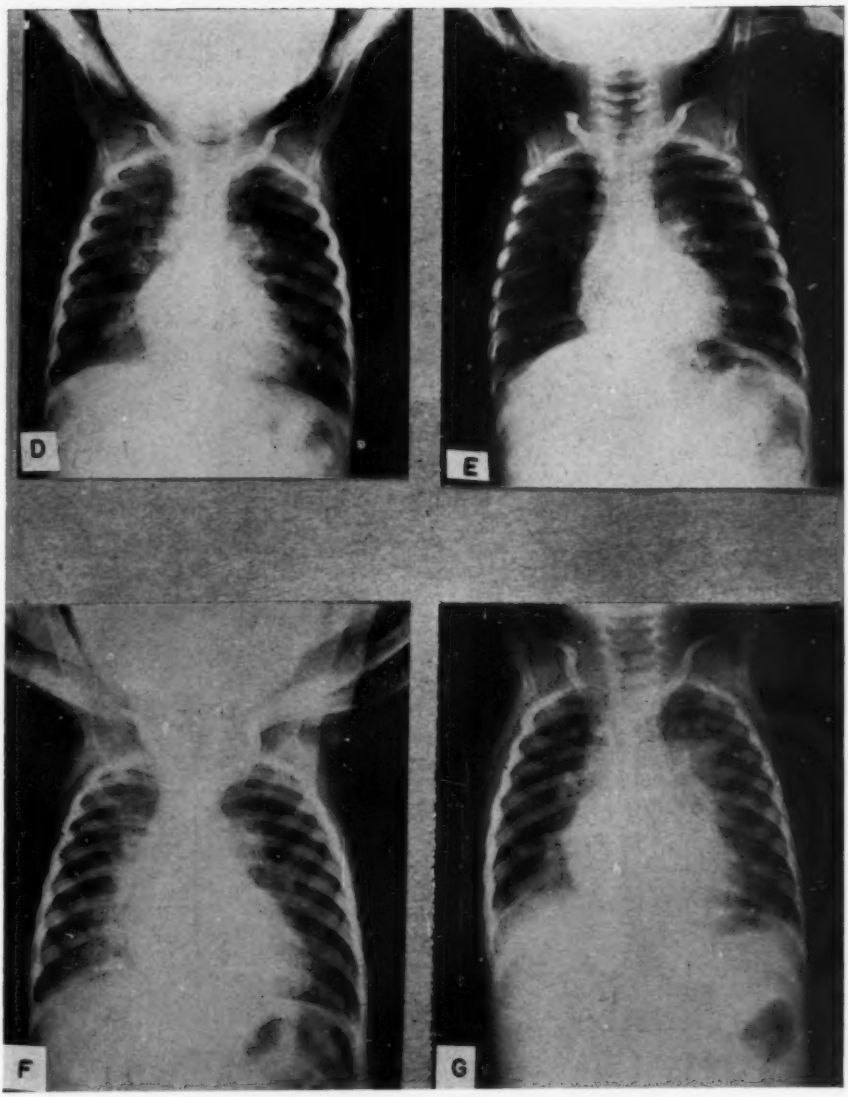

PLATE X *Cont'd.—For legend see opposite page.*

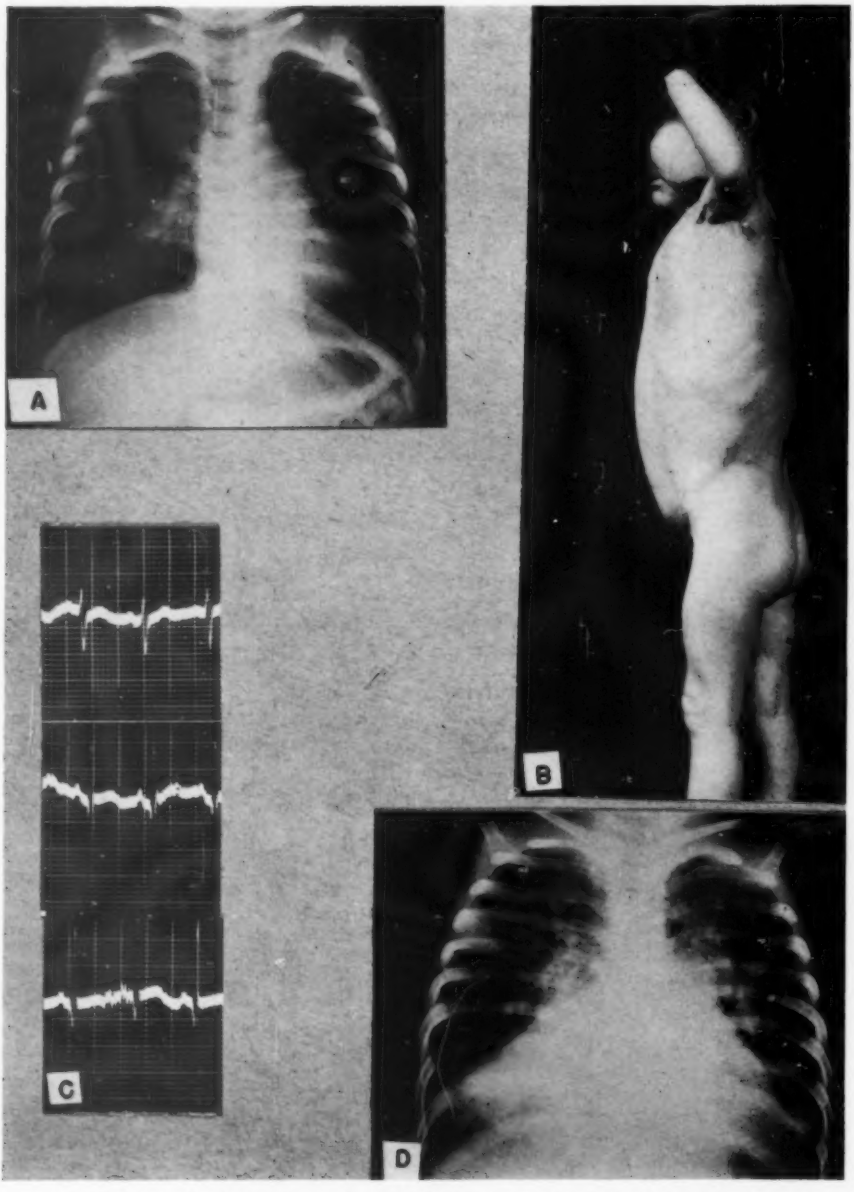

PLATE XI.—J. G., *A*, Heart and lungs at 8 months. *B*, Patient at 12 months. *C*, electrocardiogram at 17 months. *D*, Heart and lungs at 17 months.

The most extreme example of heart failure was encountered in a patient who had severe emphysema and marked infection. Respiratory embarrassment was increased by massive atelectasis. Ascites never developed, and the amount of edema varied considerably during the last three weeks of life. An electrocardiogram showed right axis deviation.

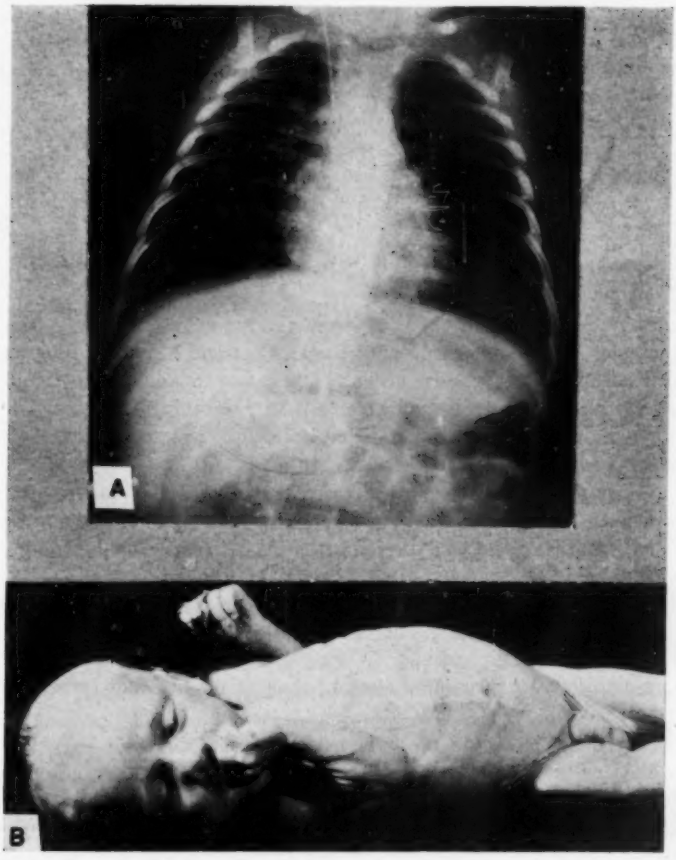

PLATE XII.—L. P., *A*, Lungs at 4 months. *B*, Patient at 4 months.

Patients surviving meconium ileus for any appreciable time develop pulmonary lesions like other individuals with fibrosis of the pancreas. This child had an ileostomy performed soon after birth, and lived to be 5 months of age, only to succumb to his pulmonary lesion. X-ray of his chest demonstrated emphysema and mild peribronchial infiltration.

scopic finding. Râles, coarse and sticky, are common, frequently persisting in one area for long periods of time. When infection is superimposed the râles are likely to be more numerous and sibilant in character. A striking feature is the discrepancy between the symptoms, which may be flagrant, and the physical findings, which are meager. Often only a roentgenogram reveals the true extent and severity of the pulmonary lesion. The lungs are invariably found to be involved by either physical examination or roentgenogram and almost always in a very widespread fashion.

The roentgenogram proves to be only a more sensitive index of pulmonary changes, particularly emphysema.[27, 28] It is particularly helpful in visualizing the degree of peribronchial infiltration during periods of infection. Viewing

the roentgenogram alone, it is often impossible to construct an accurate picture of the clinical state of the patient or to predict his progress. The clinical and roentgenologic observations together give a clearer conception of the dynamic nature of the process.

The role of infection is most readily discerned by noting the improvement in the clinical course of the patient induced by therapy directed at infection in the lungs. This has been the subject of an extensive report.[26] It seems that only a variable degree of superimposed infection in the lungs adequately accounts for the clinical phenomena. Likewise, it is clear that a basic pulmonary lesion, such as altered secretions, exists, and its progress determines the ultimate clinical course of the patient.

The unique character of the reaction of the lungs to *S. aureus* in the bronchi and bronchioles has already been mentioned. Classical *S. aureus* pneumonia and gross abscess formation rarely occur. Only two of our patients developed *S. aureus* empyema. Even bronchiectasis is surprisingly rare. Only one of the bronchograms done in eight patients with chronic pulmonary lesions revealed bronchiectasis (Plate II).

It appears at times from clinical examination that the element of infection is insignificant. The basic pathology alone appears to produce cyanosis so severe that the patient dies from anoxia. Whether this is due alone to plugged bronchioles, to bronchiolar spasm or to both, remains to be determined. The terminal illness is usually characterized by lethargy, anorexia, normal or subnormal temperature, slight leucocytosis, cyanosis not relieved by oxygen, and a roentgenogram showing severe emphysema. When this type of emphysema is complicated by a more significant degree of infection, the patient becomes feverish and even more desperately ill.

Mention must be made of a dramatic complication we have seen in six patients. After many months of severe dyspnea and cyanosis, accompanied by marked emphysema and widespread lobular atelectasis, the heart became enlarged. The cardiac enlargement may appear in the course of a few days. The enlargement of the heart appears to be due to dilatation at first as it may return equally rapidly to its normal size. But, if the pulmonary situation does not improve, the cardiac difficulty soon returns and hypertrophy develops. Other signs of congestive failure may appear along with the cardiac enlargement. Edema is at times the presenting sign, and ascites has been seen to develop. At first, one might suppose this to be due to a low serum protein concentration resulting from the deficient nutritional state. However, the amazing fact is that most patients have been found to have normal serum proteins and hemoglobin concentrations even when very wasted.[33] The albumin-globulin ratio may be undisturbed. Thus, when edema appears in these patients it is likely to be cardiac in origin. Specific deficiencies of vitamins might be considered either causative or contributory, but large amounts of all the B complex of vitamins given parenterally or orally have had no clear or lasting influence on the course of the cardiac process. Electrocardiograms in various phases of the cardiac complication sometimes show marked right axis deviation, sinus tachycardia, elevation of S-T take-off suggesting myocardial failure, or alteration in the P-R interval. We are inclined to view this cardiac complication as an example of

cor pulmonale. Cor pulmonale appears as a natural consequence of the pulmonary lesion in its severest chronic form and the dynamic concept denies the necessity of singling this group out as a "type." Detailed pathologic and physiologic studies are sorely needed to clarify this interesting and disturbing complication.

A rational therapy of the pulmonary process must be directed at both the thick secretions and the superimposed infection. Aerosol inhalation of antibiotics has been the first substantial advance in the amelioration of the pulmonary process.[25] Again and again the condition of the lungs and the clinical well-being of the patient have been improved when the infection present has been one which yields to such therapy. Clinicians have placed considerably more importance on this response than have the pathologists. We are insistent that, until the basic pathologic process is relieved, the control of the superimposed infection is only ameliorative. Unfortunately, no direct approach to the correction of the abnormal mucous secretion has as yet been devised. We have experimented, in a preliminary way, with the inhalation of substances calculated to liquefy this fiscid secretion, with encouraging results. However, close scrutiny of the roentgenograms and physical findings must be demanded whenever a claim is made that the pulmonary lesion has been "cured." Diminution of symptoms and grosser findings are frequently seen in periods of remission but never entirely normal lungs as determined by roentgenogram. We have gradually acquired the clinical impression that the pulmonary process has its inception soon after birth and builds up to a climax of activity some time afterward, usually reaching its most disturbing intensity between 6 and 18 months of age. If this period is survived, the intensity of activity of the pulmonary process seems to subside and those children who have lived 5 to 8 years are often almost free of pulmonary complaints even though once severely affected.

THE NUTRITIONAL STATE

The foregoing considerations prepare one to accept the thought that the nutritional state is hardly an independent feature of this disease. The increase in intake of food resulting from increased appetite and adaptation to a lack of pancreatic enzymes may suffice to preserve the nutritional state unless it is undermined by the deleterious effects of infection, loss of appetite, or severe pulmonary disease with cyanosis. Any degree of malnutrition, or a striking preservation of nutrition, may, therefore, be expected, depending on the severity of the basic lesions of the disease. It is inaccurate to consider the tiny scrawny infant as the "type" demanded for fibrosis of the pancreas. All basic manifestations of the pancreatic and pulmonary lesions must be allowed full weight in the diagnosis and in the evaluation of the nutritional state.

There is no convincing evidence that the pulmonary lesion can be prevented or halted in its development by improvement in the nutrition alone. Rather, the nutritional state may depend to a great extent on the pathologic changes in the lungs. If the pulmonary lesion has never been conspicuous, the nutritional state and growth may not be appreciably disturbed, even if the signs of pancreatic insufficiency have been present since birth. No one can deny that it would be better to face infection in a well-nourished condition. But, no unique

or specific causal relationship between the nutritional state and the basic pulmonary lesion has been demonstrated. It is imperative to recall the other factors that we have mentioned which by their balance determine the nutritional state.

Above all, the physician should be wary of subtracting items of food from the diet on the basis of "suspected" intolerance. One is more likely to interfere with the natural compensation of increased intake by withdrawing food for which the patient is eager. Attention had better be directed to the provision of a complete, well-balanced diet in amounts calculated to satisfy the appetite.[26] One should not become guilty of treating the stools rather than the child.

CONCLUDING COMMENTS

Sympathy is felt with those who weary of exhaustive descriptions of this disease. Yet such delineations must serve to get the stage set for the more exciting event, discovery of the actual cause. Limited attempts to reproduce the disease in animals have brought but equivocal results.[30] The common hypotheses regarding etiology which relate it to infection, nutritional deficiency, disturbed function of the autonomic nervous system, or allergy, have not as yet enabled anyone to pry out the secrets of pathogenesis. It is clear that the disease is hereditary in origin, being a Mendelian recessive characteristic.[31-33] Baggenstoss[34] has added an intriguing concept of pathogenesis, that of congenital inability of the affected individuals to produce secretin in the duodenum, with resultant inspissation of pancreatic secretion.

The validity of any classification of the disease into distinct "groups" or "types" is challenged. Selection of abstract types will only leave the bulk of patients in a "mixed" group and lure the untutored clinician into a succession of surprises as he faces natural developments. The clinical manifestations are the natural consequence of the close relation between the systems affected and the dynamic features of the disorder.

We are grateful to Dr. E. D. B. Neuhauser for his permission to reproduce the x-rays and for his guidance in their interpretation. We are deeply aware of the efforts of many of the staff of the Children's Hospital, Boston, who made the accumulation of these data possible.

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INJURIES IN CHILDHOOD

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EXACTLY how many children are disabled because of accidents has never been accurately determined. In Pennsylvania approximately 900 children lose their lives each year as the result of accidents. Nearly 12,000 children between the ages of one and 14 years die annually of accidents in the United States.

This past fall a campaign to reduce child accidents has been developed under the sponsorship of the Metropolitan Life Insurance Company in cooperation with the U. S. Children's Bureau, the American Academy of Pediatrics, and the National Safety Council. The Pennsylvania Department of Health has actively participated in this campaign.

Certain facts have been emphasized in this campaign, among which the following merit citation:

1. Accidents are the leading cause of death and an outstanding cause of permanent and disabling injuries among children more than one year of age.
2. In the past thirty-five years, the death rate from disease among children one to 14 years of age has been reduced more than 80 per cent. On the other hand, the reduction in the death rate from accidents has lagged behind.
3. After infancy, more children die as the result of accidents than from any single disease. In the ages from one to 14, inclusive, accidents take as many lives as pneumonia, diarrhea and enteritis, measles, diphtheria, meningitis, poliomyelitis, whooping cough, and scarlet fever combined.
4. Forty per cent of all accidents among children from one to 14 years of age occur in the home.
5. Burns are the cause of most fatal home accidents.
6. Falls head the list of serious nonfatal accidents.
7. Safety in the streets is extremely important, as indicated by the number of child injuries sustained through vehicle accidents. It has been estimated that more than one-third (34 per cent) of all fatal accidents result from motor vehicles.
8. A more critical attitude toward the cause of accidents is being developed by physicians and others interested in this field. There is more to injuries, especially when of a repeated nature, than "bad luck" or evil spirits. In the same way that some adults are more susceptible to accidents than others, so certain children seem to have emotional and psychic factors which predispose them to injury. In Rochester, N. Y., a clinic has been sponsored by the Medical School and the City Health Bureau to study this problem of accident-prone children and their families. Children who have been seen on more than one occasion in the accident dispensary are being studied from a physical and psychologic standpoint. Their home environment is investigated. There is a close relationship between safety and good health—not only physical health, but emotional health as well. There is evidence to show that a child who is unhappy or who lacks self-confidence may express his unhappiness, often without being aware of it, in the form of hurts and injuries to himself. The youngster who is receiving more than his share of mishaps should be scrutinized from this point of view.

9. When considering the problem of injuries in childhood, the child's personality, his muscular coordination, his physical environment, and the parents' emotional attitude toward the child are factors which merit close study.
10. Two factors characteristic of child development are frequently at the root of accidents—the desire of children to imitate others, especially their parents, and their fondness for repetition. If parents are heedless, the child may follow suit. If a child performs a hazardous act and avoids disaster, he is likely to repeat the procedure. His curiosity is liable to lead to his destruction.
11. Personality maladjustments in childhood, impaired vision or hearing, all may play a role in the accidents of childhood, particularly when repeated accidents occur.
12. The problem of child safety is one for the family and the entire community. It is rightfully a phase of public health education because accidents affect the well-being of a community. It is a subject of importance not only to the family, but to child study groups, which emphasize child hygiene, as well. Among other groups who are concerned with this problem are social agencies, city departments of health, education, police, fire prevention and housing authorities, chambers of commerce, automobile clubs, and, of course, safety councils.
13. The two outstanding causes of accidents are: unsafe conditions and unsafe practices.

With this general outline of the nature and scope of the problem we wish to consider the problem of childhood injuries from a local standpoint.

For the purpose of this study we have reviewed the records of all children 18 years of age and under who were seen at St. Luke's Hospital from June 1, 1948, to Aug. 31, 1948, inclusive. This study pertains only to those children who, following an accident, were seen at the hospital dispensary, and does not include those examined and treated by family physicians, other hospitals, or who perhaps did not require medical attention.

In this period of three months, 566 children were seen at St. Luke's Hospital for injuries sustained as the result of an accident. Four hundred two (71 per cent) were males; and 164 (29 per cent) were females. We have analyzed and investigated this group in various ways: the mechanism of the injury, the scene of the accident, the time of day the injury was sustained, and the nature of the injury have been reviewed and tabulated. We have analyzed this group with respect to the number requiring hospitalization, the number receiving antibiotics and prophylactic tetanus antitoxin or toxoid, the types of treatment that were employed, and the number requiring x-ray studies and anesthetics. Further, we have broken down several of the groups for more detailed analysis. While the time period covered in this analysis is brief (three months) the number of children involved makes the study of statistical value.

We have found that about six children a day were seen in the hospital dispensary because of an injury, and that over six children were admitted each week to the hospital for more complete therapy or study. (Table I.)

TABLE I.

Number of children 18 years of age and under	566	Male	402	(71%)
		Female	164	
Number admitted to the hospital			83	(14.6%)
Number of hospital days			646	(1 to 70)

In analyzing our patients with respect to age, it was found that more children between the age of 2 and 3 years were injured than at any other age period. The next largest group was that between the age of 5 and 6 years. (Fig. 1.)

Fig. 1.

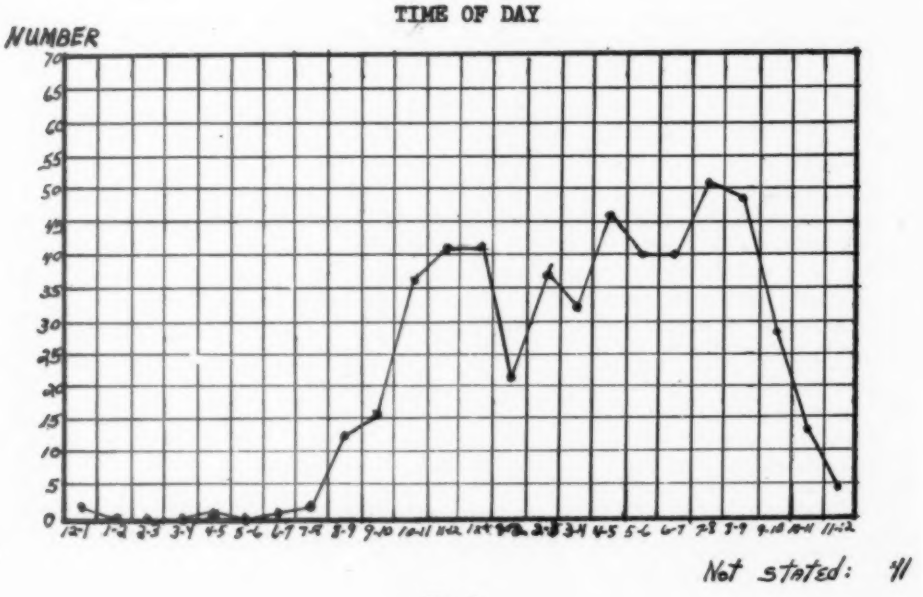

Fig. 2.

The fact that the majority of injuries in childhood occur after the noon hour is shown graphically in Fig. 2. Over 78 per cent of all accidents happen after 12 noon with the peak being between 7 and 8 P.M. However, a survey in the winter months might show the greatest number of accidents occurring at an earlier hour.

The scene of the injury is indicated in Table II. About three out of every four injuries were sustained either in or about the home or on a city street. The fact that this study was undertaken during the summer months would indicate that the number of injuries sustained in the school might be lower than a similar survey taken during the school year. The number of accidents that occurred in the hospital is explained by the use of the hospital dispensary for minor first aid to hospital employees or student nurses. Only seven accidents occurred on a farm in this series. Perhaps the country practitioner is able to treat most of these cases in his office, rather than finding it necessary to refer them to the hospital.

TABLE II. SCENE OF INJURY

Home	316	Garage	1
City street	106	Bank building	1
Playground	42	Store	1
Not stated	16	Church	1
School	16	Social hall	1
Hospital	10	Camp	2
Swimming pool	10	Woods	1
Factory	8	River	1
Farm or field	14	Bridge	1
Baseball field	4	Police station	1
Canal	3	Seashore	1
Reservoir	2	Day nursery	1
Automobile	2	Creek	1
Country club	2	College campus	1
		Total:	566

Falls accounted for almost one out of every three injuries sustained by these children. (Table III.) Considering the large number of children taking part in sports during the summer months, the number sustaining sports' injuries is not high, being only 6 per cent of the entire group. When automobile, motorscooter, and bicycle injuries are totaled, it is noted that about one child in ten becomes injured as the result of a vehicle accident. Perhaps this number would also be higher if a similar study were undertaken during the winter months when school attendance places the largest number of children on the streets at one time. A review of the miscellaneous injuries indicates that almost anything that can happen to a child usually does. He has not yet learned through experience.

Almost one-half of these children (259, or 46 per cent) were given either toxoid or antitoxin to prevent tetanus. While the value of this is questioned by some, it is considered by the surgical services of the hospital an important step in treatment. In all but the most minor injuries, tetanus prophylaxis is routinely performed, being preceded by a skin sensitivity test. In recent years

TABLE III. MECHANISM OF INJURY

Falls:		32.8%	*Playground injuries*		19
"Fell"		51	Swing, see-saw, sliding board, sandbox, etc.		
Fell from height		23	*Puncture wounds*		18
Fell on concrete, cement, sidewalk, curb, etc.		25	Sticks, pencil, pen, etc.		
Fell down steps		18	*Gun injuries*		5
Fell on glass		21	*Foreign body in eye*		9
Fell out of bed		8	*Stepped or fell on nail*		18
Fell out of chair		4	*Stepped on sharp objects*		8
Miscellaneous		36	*Splinter injuries*		2
Animal bite:		46 (8%)	*Hit by stone*		11
a. Dog	45		*Struck by door*		6
b. Cat	1		*Insect bites*		6
Sport injuries:		33 (6%)	*Toy injuries*		3
Baseball	19		*Ingestion of foreign body*		13
Other	14		Pin	4	
Wringer injuries		12 (2%)	Stone	1	
Automobile injuries		29 (5%)	Button	1	
Struck by auto	15		Iodine	1	
Bumped into car	6		Turpentine	1	
Fell off car	6		Ant poison	1	
Motor scooter		5 (0.9%)	Rubbing alcohol	1	
Bicycle		26 (3.7%)	Metal toy	1	
Carriage injuries		5	Stick	1	
Burns		21	Dress snap	1	
Electric household appliances	8		*Farm accidents*		5
Firecracker	3		*Pulled up suddenly by hand*		3
Hot fluids	3		*Tool or machine injuries*		5
Flammable liquids	2		*Knife or scissor injuries*		3
Other	5		*Not stated*		17
Swimming accidents		15	*Miscellaneous*		37
			Total:		566

no case of tetanus has been seen at the hospital in which this step had been neglected. Similarly, the use of antibiotics prophylactically is being carried out. Fifty-six of the ninety children who received penicillin were given one dose, this being 300,000 units of water-soluble crysticillin.

One out of every five children seen in this group required the use of an anesthetic, and it is interesting to note that of this number almost three out of every five received local anesthesia. A number of the fracture cases were treated by an infiltration of the fracture hematoma with procaine, and even lacerations in the older children were at times repaired under local anesthesia.

TABLE IV. ANESTHETICS

General anesthesia:			
Nitrous oxide	8		
Ether	39		
Pentothal	1	Total:	48
Local anesthesia:			
Novocaine	65		
Ether chloride	2	Total:	67
Total number of children receiving anesthetic			115 (20%)

One out of every three children (183 in all) examined this past summer at the hospital for injuries had radiographs and in eighty-two instances, there were positive findings. The large number of negative findings might be reduced if all children were examined by more experienced surgical residents. The facili-

ties of the x-ray department are open constantly, and radiographs are employed almost entirely to the exclusion of fluoroscopic examinations.

The large number of fractures of the upper extremity seen in this study is noteworthy. Fractures of the radius and ulna, either alone or together, constituted the greatest single group of fractures seen in children, amounting to twenty-nine of a total of seventy-one with fractures.

A grouping of the diagnoses is presented in Table V.

TABLE V. DIAGNOSES

Lacerations	205
Contusions	53
Puncture wounds	60
Abrasions	38
Fractures and dislocations	79
Sprains	23
Foreign bodies	24
Concussion of brain	19
Burns	21
Negative	11
Cellulitis	11
Subluxation of joint	2
Lacerated tendons	4
Not stated	9
Avulsion of fingernail	4
Miscellaneous	3
Total:	566

The repair of lacerations by sutures was carried out in 125 cases (Table VI). Although the total number of treatments is only 370 for this group, it is assumed that various other therapeutic measures may have been performed and not noted on the hospital dispensary records. Eleven major surgical procedures were required in this group. [Laparotomy, craniotomy, arthrotomy, excision of loose bone from the elbow region, amputation of finger, open reductions of fractures (two), and suturing of lacerated tendons (four).]

TABLE VI. TREATMENTS

Sutures	125	Open reduction of fracture	2
Skin clips	1	Stomach lavage	2
Ointment and dressing	33	Decompression of nail bed	2
Dressing	52	Strapping	15
Cast	32	Reduction of dislocation	1
Reduction of fracture and cast	18	Arthrotomy of knee	1
Splints	17	Laparotomy	1
Removal of foreign body	14	Craniotomy	1
Cauterization	18	Traction	1
Débridement of burns	8	Excision of loose bone	1
Incision and drainage of abscess	6	Amputation of fingertip	1
Cleansing of wound	6		
Suturing of lacerated tendon	4		
Sling	6		
Reduction of nose fracture	2	Total:	370

CHILDREN UNDER ONE YEAR OF AGE

The types of injuries sustained in children under one year of age are variable. In this group (Table VII), there were three instances in which no injury had been sustained. The number of burns sustained by infants points toward carelessness on the part of the mother.

TABLE VII. ANALYSIS OF CHILDREN UNDER ONE YEAR OF AGE

Number	14		
Age	From 2½ to 10 months (Average: 6 months)		
Scene of injury	Home in all cases		
Diagnosis:			
No injury	3	Concussion of brain	1
Burns	3	Foreign body in eye	1
Puncture wounds	2	Contusion	1
Lacerations	2	Subluxation of joint	1
Mechanism of injury:			
Fell out of crib	3		
Fell from high chair	1		
Bitten by cat	1		
Pulled up suddenly by hand	1		
Carriage rolled down steps	2		
Coffee spilled over feet	1		
Hot water spilled on hand	1		
Head bumped rusty nail	1		
Leg was wrenched	1		
Electric hot plate burn	1		

An analysis of the wringer injuries (Table VIII) is of interest in that ten of these twelve children had x-rays and in every instance the radiograph was negative for bone injury. In only one case was there a laceration, all other children sustaining contusions. As would be anticipated, the average age of this group indicates that the preschool child is the one most likely to sustain a wringer injury.

TABLE VIII. WRINGER INJURIES

Number of cases	12
Average age	4 years (2-10)
Time of day	10:30 A.M. average time for group
X-rays	10 patients (all negative)

It was interesting to note that the average time of injury for the children sustaining dog bites was 4:00 P.M., and only five occurred before the noon hour. The types of injuries sustained are indicated in Table IX. For the most part,

TABLE IX. ANALYSIS OF DOG BITE GROUP

Number of patients		45
Age		7.4 years (average)
Time of day		4 P.M. (average time: only 5 before noon)
Scene of injury:		
Home	17	
Street	19	
Neighbor's home	3	
Miscellaneous	4	
Not stated	2	
Diagnosis:		
Puncture wounds	17	
Lacerations	17	
Abrasions	10	
Contusions	1	
Part of body involved:		
Scalp and face	14	
Trunk	5	
Upper extremity	10	
Lower extremity	16	

a review of these records indicates that none of the puncture wounds, lacerations, or abrasions were of significance, although cauterization was carried out in eighteen cases.

The value of the State legislation prohibiting the use and sale of firecrackers is demonstrated in Table X. Only three children this past summer were seen at the hospital for injuries sustained as the result of playing with firecrackers. While we have no statistics to indicate what percentage reduction this is as compared to fifteen years ago, it would appear that this type of injury has become a negligible one. The burns that were sustained in the hospital, four in number, occurred either among kitchen employees under the age of eighteen years burned by heating units or by student nurses in the training school laboratory.

TABLE X. ANALYSIS OF BURNS

Number	21
Average age	8.8 years (3 under 1 year)
Average time of day	3:45 P.M.
Scene of injury:	
Home	15
Hospital	4
Factory	1
Seashore	1
Types of burns:	
Electric household appliances	8
Firecrackers	3
Hot fluids	3
Sunburn	2
Flammable fluids	2
Acid	2
Not stated	1
Total:	21

It is apparent from the analysis of the automobile injuries that boys are involved more often than girls and this group constitutes the number with the most serious injuries, there being nine fractures and three concussions reported. The mechanism of the injury and the scene of the injury are itemized in Table XI.

TABLE XI. ANALYSIS OF AUTOMOBILE INJURIES

Number	27
Average age	7.5 years
Time of day (average)	4 P.M.
Scene of injury:	
City street	18
Home	3
Road	2
In auto	2
Picnic grove	1
Not stated	1
Mechanism of injury:	
Struck by	15
Fell from	6
Bumped into	6

Bicycle and motorscooter injuries, thirty-one in number, are analyzed in Table XII. The age group here is higher than in the automobile injuries, being 9.3 years for the group.

TABLE XII. BICYCLE AND MOTORSCOOTER INJURIES

Number	31
Average age	9.3 years
Time of day	5 P.M. (only 3 before noon)
Mechanism of injury:	
Fell from	21
Pedal injury	5
Struck by car	3
Scared by car	1
Not stated	1
Scene of injury:	
City street	18
Home	10
Playground	2
Not stated	1

Of all of these children 13.3 per cent sustained fractures. Such injuries were twice as common in boys as in girls, and of the seventy-five children with fractures who were analyzed, twenty-six were admitted to the hospital; thirty-three required an anesthetic. The average time of day before and after the noon hour is indicated in Table XIII, and the mechanism and scene of injury are likewise analyzed here.

TABLE XIII. ANALYSIS OF FRACTURES

Number	75	
Average age	8.8 years	
Time of Day:		
Before noon	15	(Average time: 10:15 A.M.)
After noon	57	(Average time: 6:15 P.M.)
Not stated	3	
Mechanism of injury:		
Fell from height	19	
"Fell"	12	
Sport injury	14	
Auto injury	9	
Bicycle injury	7	
Fell from horse	2	
Hit by fist	2	
Miscellaneous	10	
Scene of injury:		
Home	29	
Street	20	
Playground	15	
School	4	
Farm	3	
Factory	1	
Miscellaneous	3	
Total:	75	

SUMMARY AND CONCLUSIONS

1. That 566 injured children were examined and treated in the accident room of St. Luke's Hospital in Bethlehem in a three-month period indicates that the problem of child safety is one of sufficient magnitude to warrant continued and more detailed study.

2. Of the accidents last summer, 55.8 per cent occurred in the home and 18.7 per cent on one of the city streets.

3. It was necessary to admit 14.8 per cent of the patients to the hospital for further treatment or study.

4. There were no deaths from injuries in the group of children reviewed for this study.

5. More injuries occurred in children between 2 and 3 years of age than at any other age. The next largest group was that between 5 and 6 years. 62 per cent of all children analyzed in this study were 9 years of age or under.

6. Seventy-eight per cent of all injuries occurred after noon, with the largest number of accidents occurring between 7 and 8 P.M.

7. Concerning the mechanism of injury in this series, it has been demonstrated that injuries result from:

Falls	32.8 per cent
Animal bites	8 per cent
Sport injuries	6 per cent
Automobile injuries	5 per cent
Bicycle injuries	4.6 per cent
Burns	3.7 per cent

8. Twenty per cent required an anesthetic and in those instances in which one was employed, in 58 per cent of the cases local anesthesia was administered.

9. Thirty-three per cent required x-ray study.

10. In 64 per cent of the cases, lacerations, contusions, abrasions, and puncture wounds were the primary diagnoses. In 13.3 per cent the diagnosis was a fracture of a bone.

11. It is virtually impossible to analyze a group of this type from the standpoint of end results. However, a careful examination of the hospital records would indicate that the vast majority of these injuries were not of a serious nature. It would be our impression that injuries are not a major cause of crippling from a percentage standpoint. We are unable, however, to support this feeling statistically at this time.

12. Two thoughts are developed from this study:

(a) The large number of children who go directly to the hospital dispensary for treatment apparently by-passing the family physician; (b) The service which the hospital unfailingly renders to the community in being prepared day or night to accept these injured children for any type of therapy no matter how slight or drastic, and to have available twenty-four hours a day all facilities so necessary to prompt and efficient treatment. Physicians, nurses, technicians, and orderlies are always on call with adequate reserves. The use of the operating room, the x-ray department, the blood bank; the availability of antibiotics, tetanus prophylaxis, opiates, stimulants, and special instruments, is a source of wonder even to those who work day in and day out in this environment.

13. Finally, figures are impersonal, and do not disclose the personal and family tragedies covered by these numbers which seem to rise higher year by year. One writer states that, "we have conquered pestilence and are eliminating the life-destroying infectious diseases of the past, but we permit the automobile, the modern plague which has turned our highways into roads of disaster and

death, to erase our victories." Our record of injuries, even in childhood, is a terrible record, and it becomes all the more depressing when we remember the estimate of the Traveler's Insurance Company that 98 per cent of all accidents can be prevented.

We would submit for consideration that a special committee to study this problem locally, headed by a pediatrician, might be of immense value to the community.

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SEROTHERAPY IN PERTUSSIS

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THOUGH a preventable disease, whooping cough still affects large numbers of infants and children in many sections of this country where the practice of preventive medicine has not kept pace with scientific progress. The disease is well known to be of grave import in the infant under 6 months of age in whom immunization has not generally been practiced, because of the prevailing opinion that the mechanisms for producing active immunity in this age group are immature.[1] The validity of this opinion is to be doubted, however, in the light of recent studies relative to pertussis immunization in early infancy.[2, 3, 4]

The challenge of a common disease in infancy associated with high mortality and with immediate as well as late pulmonary and possibly central nervous system complications has resulted in many studies related to specific therapeutic agents against active pertussis during the past ten years. Despite great advance in antibiotic therapy which has been shown to be very effective against the frequent and serious bacterial complications of this disease, the primary agent has not yet been conquered. Suggestive experimental studies with streptomycin have been made[5, 6] and clinical evaluation with this agent is in progress but not yet reported. Many studies relating to the effectiveness against whooping cough of specific antiserum of both human and animal origin have been published in the past ten years with uniformly favorable conclusions where hyperimmune human serum was used but with far less enthusiasm for the efficacy of rabbit serum.

The present study was undertaken with the view of comparing the effectiveness of three types of antisera with each other, as well as with concomitant controls. The diagnosis of whooping cough was based primarily on clinical grounds and substantiated in the great majority of instances by the characteristic lymphocytic response, or by positive nasopharyngeal cultures in the few questionable cases.

The plan of study was essentially to treat patients with cases of similar severity and duration in the same age groups with the three types of therapeutic sera, and to secure a more or less simultaneous group of similar untreated controls. It was impossible to alternate cases for treatment and control because of the marked variation in severity, age, and duration of disease on admission, and because of the variability of the supply of the various sera. Nevertheless, it is felt that with detailed histories and careful observation of

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the patients' course and condition during the first two to five days of hospitalization, together with pertinent laboratory and x-ray studies, we were enabled to place the cases in rather definite categories, so that within a given period of one to two weeks at least one or more patients of similar age, severity, and duration of disease could be placed in each of the four divisions of the study.

With a view to evaluation of results certain procedures were followed in all cases, and included all criteria used in previously published reports so that some common denominator might be at hand whereby comparisons might reasonably be made. Thus, severity of illness on admission was determined by the history, duration, frequency and severity of paroxysms, the state of nutrition, frequency of vomiting, episodes of cyanosis, and degree of pulmonary involvement. In almost every case a period of two to five days elapsed after admission during which there was ample opportunity to gauge the overall picture of the illness, particularly with reference to the severity and frequency of paroxysms, whoops, periods of cyanosis, and vomiting. All of these were rather accurately charted by the nursing staff, which was instructed concerning the importance of these observations and the charting throughout the patients' entire hospitalization. They had no preconceived notions as to the efficacy of any of the sera being used. Throughout the period of study at least one of us was in fairly constant attendance on the wards, and we feel that though a goodly number of paroxysms were unobserved or uncharted, especially at night when the nursing staff was cut down, nevertheless, a great majority of these were recorded and constituted what is probably the single most objective clinical estimate of the severity and progress of the illness.

Additional observations which appeared pertinent to the study included patients' weights on admission and twice weekly thereafter, chest roentgenograms on entry and at weekly intervals during hospitalization, frequent agglutination studies on most of the treated patients and on several of the controls, and finally hemoglobin estimations together with white cell and differential counts on all patients at the time of admission and once weekly thereafter.

This series comprises a total of 150 consecutive cases of pertussis admitted from October, 1946, through December, 1947. Of these, forty-eight were untreated controls, thirty-eight received a refined horse hyperimmune serum,* thirty-three received a refined, concentrated, globulin fraction obtained from the serum of rabbits which had been immunized repeatedly with killed cultures of Phase I *Hemophilus pertussis* as well as a pertussis endotoxoid,† and thirty-one received a concentrated globulin fraction prepared from human hyperimmune serum.‡ All treated patients in the series were in the paroxysmal stage of the disease.

Table I indicates age distribution and type of serum employed in the various patient divisions.

*Supplied by Lederle Laboratories.
†Supplied by Ayerst, McKenna, and Harrison Ltd., Montreal, Canada
‡Supplied by Cutter Laboratories, Berkeley, Calif.

TABLE I. ADMISSIONS FOR WHOOPING COUGH, OCTOBER, 1946, TO DECEMBER, 1947, WITH AGE DISTRIBUTION AND TYPE OF SERUM THERAPY

AGE	TOTAL ADMISSIONS	HUMAN SERUM	RABBIT SERUM	HORSE SERUM	CONTROL
0-6 months	31	9	6	6	10
7-12 months	37	8	9	12	8
1-8 years	82	14	18	20	30
Total	150	31	33	38	48

DOSAGE

Horse Antipertussis Serum.—At the beginning of the study single doses of 10,000 to 20,000 units intramuscularly were used, the smaller doses for the younger infants. When these appeared to be ineffective the dose was increased to as high as 75,000 units, the average dose for all patients being 40,000 units. The usual precautions taken in all foreign serum therapy were carried out, and the only reactions which appeared were two instances of transient urticaria. The great majority of patients received the entire amount in one injection, the remainder receiving no more than two injections on consecutive or alternate days.

Rabbit Antipertussis Serum.—At the outset single doses of 10,000 units intramuscularly were employed. Ineffectiveness of this dose seemed apparent early in the study, and subsequent doses were scaled to as high as 75,000 units in the more severe and older patients, the combined average among all patients being 40,000 units. Again practically all patients received the entire dose in one injection, the remainder receiving no more than two doses at one- or two-day intervals. No untoward reactions to this serum were noted.

Human Hyperimmune Antipertussis Serum.—Of this 2.5 c.c. are equivalent to 20 c.c. of the original serum. The dosage varied from 2.5 c.c. (two cases) to 10 c.c. (ten cases), with an average of 7.5 c.c. Twelve patients received two injections on successive days, the remainder received the entire amount in one dose. There were no local or systemic reactions to this serum.

RESULTS

Following are figures representing summary of course of the disease. Figures are averages obtained from individual charts.*

	CASES TREATED IN FIRST WEEK			CASES TREATED IN SECOND WEEK			CASES TREATED IN THIRD WEEK		
	A	B	C	A	B	C	A	B	C
Controls	7	24	22	7	28	21	5	27	15
Horse serum	6	25	18	6	29	19	5	44	27
Human serum	6	26	22	3	28	17	4	39	33
Rabbit serum	11	33	29	5	30	20	8	51	37

*A, days after treatment that the peak of the disease was reached (or the days after entry in the controls).
B, the total duration of the paroxysms in days.
C, the duration after treatment (or after entry in the controls), in days.

Examination of the above figures fails to reveal any marked difference in the clinical course of the four groups of patients. A breakdown of the cases

according to the dosage of serum used fails to show any difference in those patients treated with larger doses or with multiple doses.

Table II shows the distribution according to severity, with subsequent courses judged on the basis of definite improvement, no improvement, or worsening of condition. Improvement was based on decided decrease in coughing and vomiting within three to four days after serum therapy, and on improvement in appetite and general appearance of the patient.

TABLE II. DATA ON SEVERITY ON ADMISSION, WITH RESULTS OF SERUM THERAPY

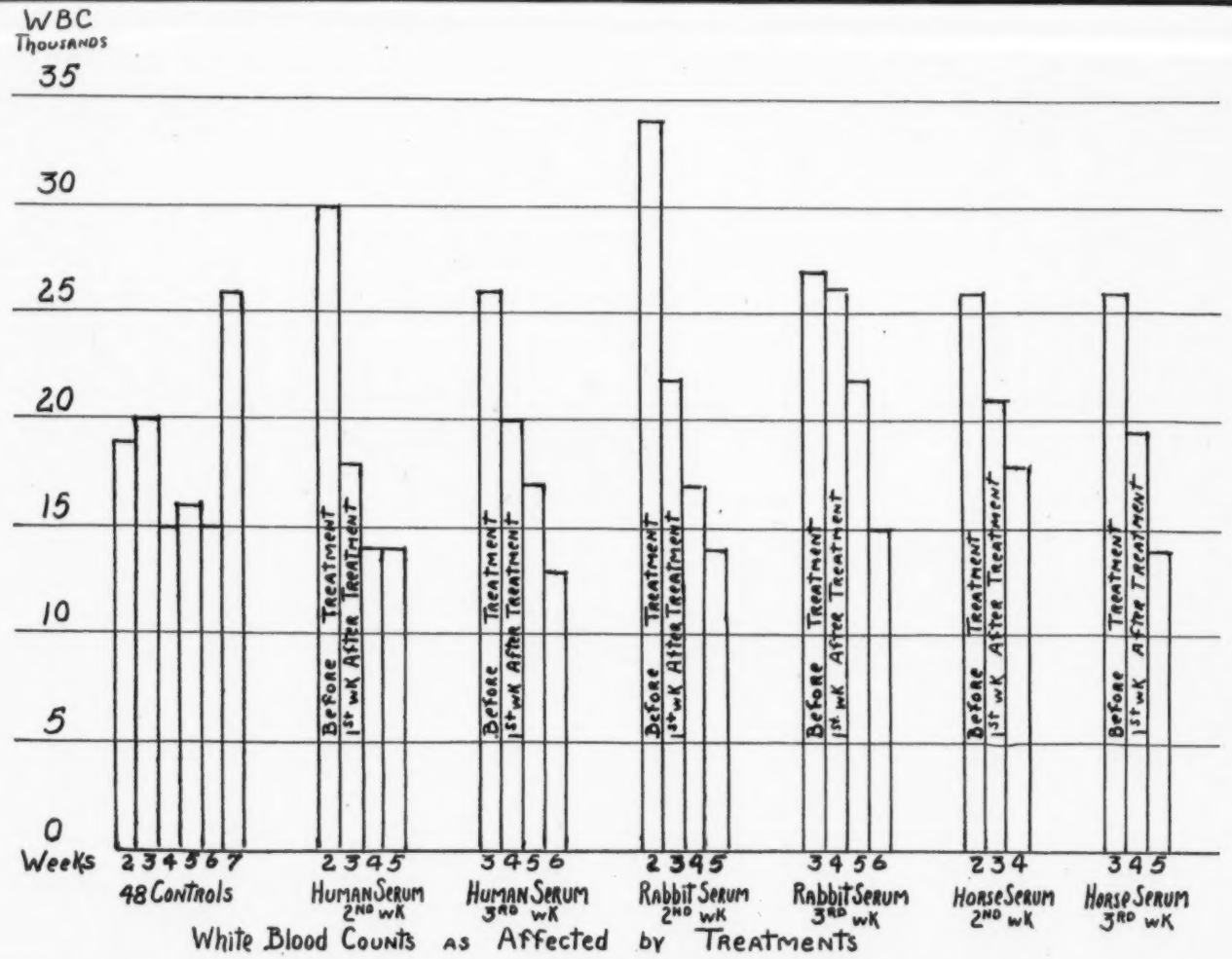
AGE	SEVERITY OF DISEASES ON ADMISSION			SUBSEQUENT CONDITION		
	MILD	MODERATE	SEVERE	IMPROVED	UNCHANGED	WORSE
Human Serum						
0-6 months	2	5	2	—	9	—
7-12 months	1	7	—	1	7	—
1-8 years	4	7	3	—	12	2
Rabbit Serum						
0-6 months	2	4	—	—	5	1
7-12 months	3	5	1	—	9	—
1-8 years	3	10	5	3	14	1
Horse Serum						
0-6 months	1	5	—	1	3	2
7-12 months	4	7	1	1	10	1
1-8 years	4	7	9	1	17	2
Controls						
0-6 months	5	4	1	1	6	3
7-12 months	4	3	1	—	7	1
1-8 years	15	12	3	4	22	4

A breakdown of the above cases according to the week of disease in which serum treatment was given does not indicate any significant differences in response of patients treated early or late.

Some of the previously reported series treated with human hyperimmune serum have emphasized the occurrence of a significant decrease in lymphocytosis shortly following therapy.[7, 8, 9] Chart 1 illustrates the averages of absolute lymphocytosis among the four groups of patients, with weekly changes after serum therapy or after admission among the controls. Chart 2 illustrates the findings in a group of seventy untreated patients followed from the inception of the disease.[10] Initial counts among our controls are lower than in the treated cases, this being due, we feel, to the fact that the control series contained more of the mild cases. In general, the degree of lymphocytosis correlated well with the number and severity of paroxysms, the higher counts accompanying the more severe symptoms. The charts agree well with the studies previously mentioned in that significant decreases in lymphocyte counts occurred within one to two weeks following serum therapy at periods of the disease in which rising counts would ordinarily be anticipated. However, these decreases, though very marked in some instances, did not correlate at all with significant lessening of paroxysms or vomiting, even among the few patients that could be classed as improved.

One further study was made in an effort to obtain more objective evidence of the effect of serum therapy in relation to the course of disease, this consisting of agglutination studies in several of the untreated and many of

WBC Thousands


WBC
Thousands
35
30
25
20
15
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Weeks
2 3 4 5 6 7
48 Controls
2 3 4 5
Human Serum 2nd wk
3 4 5 6
Human Serum 3rd wk
2 3 4 5
Rabbit Serum 2nd wk
3 4 5 6
Rabbit Serum 3rd wk
2 3 4
Horse Serum 2nd wk
3 4 5
Horse Serum 3rd wk
Before Treatment
1st wk After Treatment
White Blood Counts as Affected by Treatments

Chart 1.

the treated patients both before and at frequent intervals following treatment. The accompanying Chart 3 illustrates these findings.

A very good titer rise is apparent within twenty-four hours of any type of serum therapy, with rapid falling off among the horse and human serum treated cases, but with maintenance of better titers than among the controls in all treated cases for at least two weeks after serum treatment. Titers drawn in the third and fourth weeks of the paroxysmal stages must represent not only passively transferred antibody but also the patients' own active production of antibody at this stage of disease, as shown among the controls which have the expected titers at this period, but in lower concentration than the treated cases.

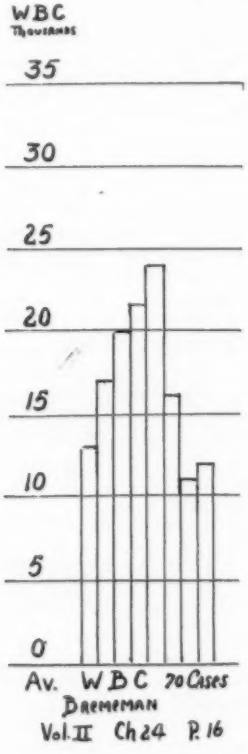

Chart 2.

In analyzing individual cases, it was evident that the higher initial titers were present in the milder forms of the disease, and that these generally responded with a higher titer rise following serum treatment. Patients who were given the larger doses of serum generally had the higher agglutination rises, but there were several instances in which relatively small dosage of any of

the types of sera resulted in significant immediate and sustained agglutination titer rises. In no instance was it clear that definite improvement occurred among those patients with excellent agglutination responses, and as a matter of fact most of those who were judged improved had average or slightly lower than average agglutination responses.

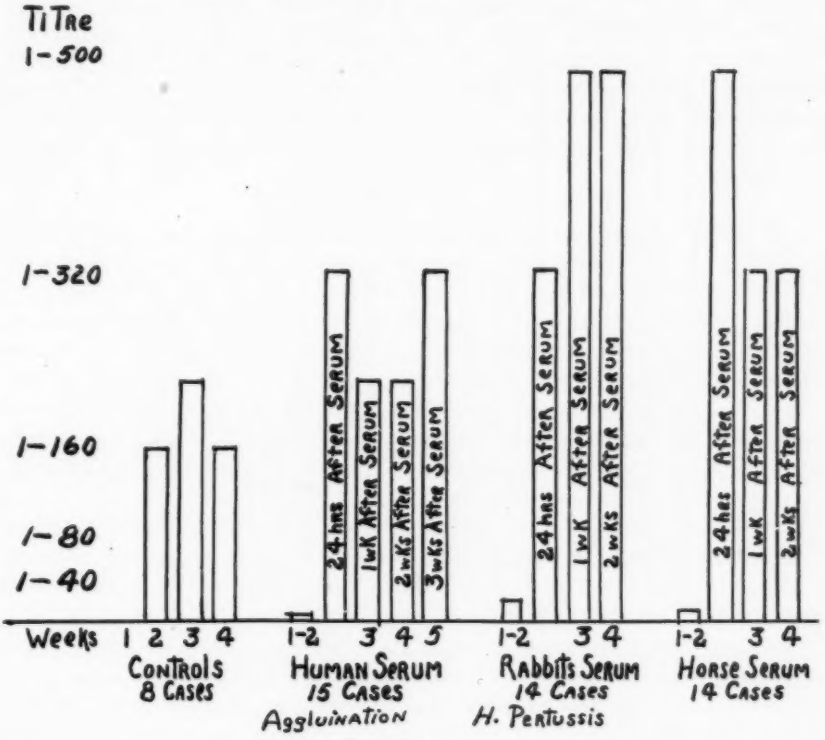

Chart 3.

Scheinblum and Bullowa,[8] using hyperimmune serum, found no correlation between response to therapy and height of post-treatment titers. Bullowa and Alterman[11] used rabbit antitoxin in treatment and found no definite improvement despite marked rise in serum antitoxin titers. Ketsampes and associates[7] found significant titer rises in twenty-two patients treated with hyperimmune human serum, but did not state specifically whether the degree of titer response could be related to the course of the patient.

Weights on all patients showed no significant variations among the treated and controls. Practically every patient gained weight while in the hospital, weight gains becoming evident almost invariably shortly after the peak of disease was reached, as would be expected in the absence of refractory complications.

Complications included pneumonia, otitis media, diarrhea, malnutrition, anemia, and two instances of transfusion malaria. Pneumonia occurred with about the same frequency in the four patient divisions, averaging 15 per cent. Only one case of pneumonia developed following serum treatment, this occurring in the rabbit serum-treated group one week following the serum. Pneumonia did not develop among any of the control patients during hospitalization. The remaining complications occurred in insignificant numbers. Of these, all but the cases of transfusion malaria were present on admission. Sulfonamides, penicillin, transfusions, parenteral fluids, and other indicated supportive therapy were used as necessary among the four groups of patients with uniformly satisfactory responses.

DISCUSSION

It is difficult to ignore the large numbers of favorable reports on the use of hyperimmune serum in whooping cough. These have been reviewed by Felton,[12] Kohn et al,[13] and recently by Brainerd[9] and Rizzo.[14] Combining figures of human serum treated cases in which patients are separated by age groups with respective mortalities, a total of 784 patients is obtained, of whom 445 were less than one year of age, with a mortality in this group of 2.4 per cent. In various groups reported mortalities ranged from none in smaller series to as high as 20 per cent in a group in which all had bronchopneumonia. The largest series is that of McGuiness and associates[15] in which the mortality rate among 236 patients less than one year of age was 2.1 per cent. Five hundred seventy-two or 73 per cent of the 784 patients were considered definitely improved by the serum. The range of patients considered improved within a few days to a week after administration of the serum in the various groups was 63 per cent to 88 per cent.

Relatively few reports on the use of hyperimmune rabbit serum have been published.[13, 16, 17, 18] Favorable results were noted in only one group, that of Beaudet,[16] the others reporting equivocal results. Becker[21] treated sixteen children in the incubation stage and twenty-five in paroxysmal stage with horse antitoxin from the Behring works. Ten of the incubation-stage cases developed the disease and there was no apparent effect of therapy in the twenty-five cases.

The great majority of the aforementioned reports have stressed the role of serum therapy in diminishing the mortality in the youngest age groups, as compared with similar cases seen in previous years. Mortality rates among nonserum treated cases in the age group under one year actually vary widely, these having been reported as low as 4.9 per cent and as high as 25 per cent.[13, 19] Chart 4 shows the mortality in the youngest age group at this hospital from 1930 to 1946, and aside from an actual mortality rate of 6.4 per cent during the years 1940 to 1945, a fairly steady decline in mortality has been notable since 1937. This coincides with the picture of over-all mortality changes occurring in Boston among all age groups beginning in the year

1936, as illustrated in Charts 5 and 6. It is to be noted that this change antedates the general introduction of the sulfonamide group of drugs and might well indicate declining severity of the natural disease, at least in this area.

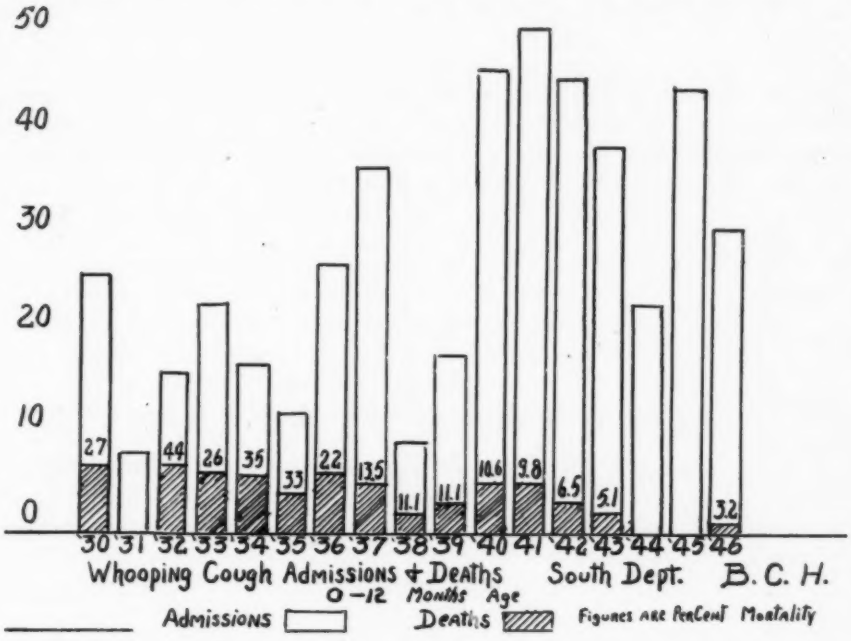

Chart 4.

Admittedly, any evaluation of a single therapeutic agent against pertussis is extremely difficult because of the marked natural variations in the severity as well as duration of the disease. Critical appraisal of results must then become especially difficult if other agents known to be effective against the most common and very serious complications of the disease are used concomitantly. Thus, antibiotics could not well be withheld in a patient seriously ill with a pulmonary complication of pertussis, and since the latter cause by far the greatest number of deaths in the disease, lowered mortality rates among patients treated with both an antibiotic and an immune serum could not easily be attributed to the latter. Thus, Frank and associates[20] found a mortality rate of 20 per cent in thirty consecutive patients with whooping cough with bronchopneumonia treated with human hyperimmune serum alone. The same authors found a mortality of 4 per cent in seventy-seven consecutive patients with similarly complicated cases treated with sulfathiazole alone. One might easily imagine a further reduction of this mortality if penicillin had also been available for pneumonia-producing organisms resistant to sulfonamides. In view, then, of the widely varying mortality figures on

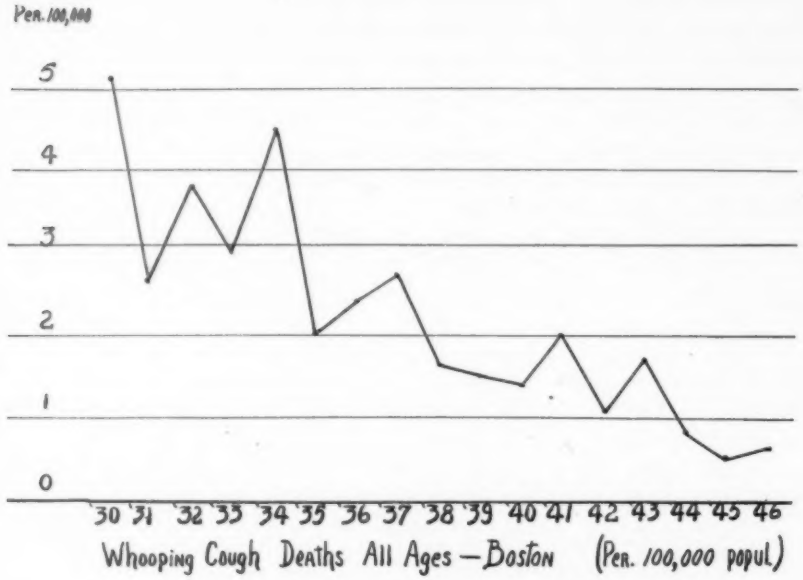

Chart 5.

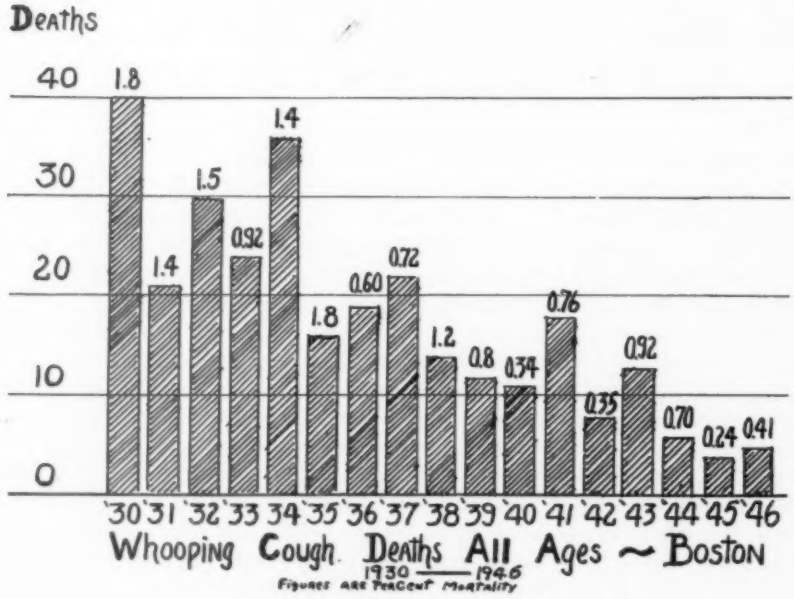

Chart 6.

whooping cough in different clinics and in the years before and after the antibiotics came into general and liberal use, extreme caution is indicated in the evaluation of any antipertussis agent based on lowering of previous figures.

Further evaluation of serum therapy as noted in previous reports has rested on impressions of marked reduction in coughing and vomiting and on improvement of the general condition of the patient. In very few of the studies was actual day-to-day charting of the frequency and severity of paroxysms carried out because of limitations of time and personnel and also because many of these patients were cared for at home. Even had this procedure been carried out, definite conclusions could not necessarily be drawn in the absence of adequate numbers of controls. Thus, in our own group of forty-eight hospitalized controls whose paroxysms, whoops, and vomiting were charted from day to day, it was often noted that several of these showed striking improvement in a given forty-eight hour period either early or late in the disease. Had serum been given just prior to one of these spontaneous changes, erroneous conclusions as to serum effect could easily be drawn.

The fact that pulmonary complications have very rarely been seen following serum therapy has also been stressed as an indication of the effectiveness of serum. Our study does not indicate this to be necessarily due to serum therapy, since none of the controls developed a pulmonary complication after hospitalization.

Multiple dose serum therapy has been used in the large majority of reported cases, but evidence that this is more efficacious than single large doses has not been advanced. It appeared logical to assume that if no demonstrable clinical effect could be obtained with a single large dose, which, in over 90 per cent of our cases, was equivalent to the total multiple dose treatment recommended, i.e., 60 c.c. of the hyperimmune serum or 7.5 c.c. of the concentrated globulin fraction thereof, then further efforts along this line would not be expected to show any great difference. If prompt and significant agglutination titer rises, together with a fairly rapid fall in the total number of circulating lymphocytes, are considered an index of adequate serum therapy, then these criteria indicate results equivalent to those previously reported with multiple dose therapy where these factors were utilized as a more objective index of response to serum treatment.[7, 8 9, 11]

CONCLUSIONS

1. One hundred fifty consecutive hospitalized patients with pertussis in the period October, 1946, through December, 1947, were studied with a view to evaluation of various types of specific serum therapy. Thirty-eight patients received horse serum, thirty-three a hyperimmune rabbit serum, thirty-one human hyperimmune serum, and forty-eight patients were used as controls.

2. There were no deaths in any of the four groups.

3. On the basis of day-to-day charting of paroxysms and vomiting, weight changes, and general appearance of patients, no significant differences in the clinical courses of any of the patient groups was evident.

4. Significant reductions in absolute lymphocytosis as well as good rises in serum agglutination titers followed serum therapy, but these changes did not correlate with clinical improvement.

5. The number of both treated and control cases is admittedly quite small, but in view of the currently held ideas as to the value of human hyperimmune serum therapy, it is felt that this study suggests the need for further more critical and controlled evaluation of the serum treatment of pertussis.

6. The lack of fatalities, though possibly influenced by serum, is more likely the result of improved therapeutic procedures relating particularly to bacterial complications and to diligent nursing care.

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EPIDEMIC DIARRHEA OF THE NEWBORN INFANT

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THERE are inherent dangers in the preparation of formula for infants. The young baby is particularly susceptible to intestinal upsets, either infection or toxicosis. In the scheme of things every baby, human or animal, should have its mother's milk. Nature provides a safe and fresh food supply in the maternal milk. If, on the other hand, we are to tamper with nature, the most rigid safeguards must be applied to the procedures of formula preparation.

These procedures should be of such a character that the day-old refrigerated food will be practically free from bacteria as determined by bacteriological culture methods. To secure this result regularly and with certainty, the formula nurse must have a knowledge of the techniques of both bacteriology and mechanics, asceptic technique and refrigeration operation.

While it is not the purpose of this paper to relate the history of infant diarrhea, it should be appreciated that in recent years great progress has been made in the control of the disease. Less than fifty years ago, one-quarter to one-third of all infants died during the first year of life. About 80 per cent of these deaths were due to "cholera morbus" or infant diarrhea. The season of greatest prevalence was during the summer months. Forty years ago the public milk supply in Washington, D. C., had an average bacterial count of 10,000,000 per cubic centimeter; today the counts are about 5,000 per cubic centimeter, a reduction of almost 100 per cent.

It was Nathan Strauss who, about the middle nineties, led the campaign for the establishment of safe milk stations for babies. But it was not until about thirty years later that he said, "I have finally won my fight for safe milk for babies." Today only about fifty infants per 1,000 die in the first year of life compared to 300 fifty years ago. All of which means that now the death rate has been reduced by over 80 per cent, or stated another way, out of every 1,000, 250 babies under one year of age are being saved annually.

In Washington, D. C., where we had 27,000 births in 1947, the lives of almost 7,000 babies were saved compared to the rate of fifty years ago. This yearly addition to the population gives something to ponder. But our interest here is the control of infant diarrhea in hospital nurseries. Observation over the last twenty years indicates that there may be two types of infant diarrhea. The numerous outbreaks of the 1930's were highly explosive in character; within a week or less, one-third or more of the infants would develop the infection. There was a high case mortality of 30 to 40 per cent. The

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disease had a sudden onset with excessive diarrhea and rapid dehydration. These outbreaks were sudden, severe, and of short duration.

An investigation undertaken in 1936 of twenty-four-hour-old bottled baby food in six of our local hospitals showed that the average bacterial count per cubic centimeter was almost 500,000, with 24 per cent of the specimens showing *Bacillus coli* contaminations; that the drainage water from the nipple container carried an average of 60,000 bacteria per cubic centimeter, and that the bottles, after having been "washed and sterilized," each carried a load of about 80,000 bacteria.

While the excessive bacterial counts in the bottled milk were not of themselves directly the cause of infant diarrhea, it at once became apparent that they kept the door open for the introduction of dangerous disease-producing organisms or viruses. The high counts prevailed continuously; an epidemic arose only when the etiologic factor was introduced from an adult carrier or other source into the bottled milk, thence spreading throughout the formula laboratory equipment.

The severity of these outbreaks during the thirties might well have been due to multiple massive doses of the causative agent in the bottled food. Since 1940, however, the formula laboratories have been well organized with counts of not more than several hundred bacteria per cubic centimeter at any time. Yet we have had several low-grade outbreaks.

Such an outbreak occurred in 1946 in a hospital in which the total deliveries for the year were 4,166. During a three-month period, there were 128 cases of diarrhea among the newborn, with but four deaths, a very low case mortality rate. In contrast to the epidemic of the 1930's, the 1946 outbreak was characterized by its mildness, its gradual onset, and prolonged duration.

Simultaneously with this infant outbreak there was a widespread epidemic of contact adult diarrhea in that section of the city where the hospital was located. Based on the number of these patients treated in outpatient clinics and those treated by private physicians, it was roughly estimated that there were about 10,000 adult cases.

The first case of infant diarrhea in the hospital during the 1946 outbreak was that in an infant born to a mother convalescent from contact diarrhea. The incubation period in the infant was two days. Within a few days there were secondary cases, all of whom were isolated. But new cases in two-day-old babies of mothers having diarrhea continued to occur from time to time; from these there were secondary contact cases. This process of introduction, spread, and isolation continued over a period of three months and involved 128 infants.

As had been the routine for a number of years the formulae were frequently checked for bacterial contamination, and, during the epidemic period, the bottled food continued to be practically sterile. There appears to be no doubt that there were secondary cases among the infants. How many is not known. These were, however, contact cases and not foodborne.

An interesting question here is whether or not the safety of the bottled food protected the nurseries from a highly fatal virulent epidemic of diarrhea. One might theorize on this question without a conclusion. But here the point is that the 1946 epidemic was low-grade, almost nonfatal, while the epidemics of the 1930's were explosive and virulent with a high mortality.

TECHNICAL ERRORS

A number of technical errors were observed during the early days of this survey, and any one of these may lead to dangerous contamination of bottled food. In the first place inadequate washing of bottles was of frequent occurrence. As already stated "washed and sterilized" bottles had an average bacterial count of 80,000 per bottle. It was then found that by thorough washing and rinsing, heavy contamination could be reduced as much as 90 per cent. Today with modern detergent powders, bottles can be rendered practically free from bacteria; they are bright, crystal clear, and free from film.

There was, secondly, the practice of piling bottles in a large pan two-thirds full of water while the bottles filled the vessel. Many were not in contact with the water. As a formula laboratory procedure steam "sterilization" is wholly inadequate. There is but one safe and dependable way to sterilize bottles—in the autoclave.

A third hazardous practice was that nurses in training were permitted to perform the technical procedure of preparing food by formula.

A fourth defect related to the use of warm stock water in making the formulae. When this investigation was started in 1936, it was the universal practice to use warm stock water. It was contended that it was more convenient to sterilize the water the morning of the day it was used, and then too, it was argued that powdered foods went into solution more readily in warm water.

It was found by automatic recording of the refrigerator temperature that when 200 bottles with their warm content were placed in the refrigerator (recording a temperature of 45° F.) there was a gradual increase for six hours to 78° F.; and during the following seven hours there was a slow drop to 45° F. Thus for thirteen hours a temperature prevailed favorable to the growth of bacteria, perhaps dangerous ones. This accounts in part for bacterial counts of over a million per cubic centimeter in twenty-four-hour bottles.

The correction here was simple: merely sterilizing gallon containers of water in the autoclave the day previous, allowing these to cool to room temperature and finally placing them in the refrigerator overnight. The use of this cooled stock water for formula provided continuous refrigeration of the bottled food. Thus bacterial multiplication was inhibited.

A fifth hazard was the neglect of defrosting. This occurred especially when there was a frequent turnover in the personnel of the formula room. It is now required that the refrigerator temperature be recorded daily at 9 A.M. and 1 P.M.

A sixth hazardous difficulty was mechanical failure of the refrigerator equipment. In 1938 there was an outbreak of infant diarrhea in one of our hospitals. On investigation, it was found that the formula nurse was gowned, capped, masked, and gloved. This created a sense of security, but behind the scene it was found that the stock water was not chilled and that the empty refrigerator registered but 72° F. Many of the 24-hour formula samples had bacterial counts of over one million bacteria per cubic centimeter. The refrigerator was replaced and the stock water chilled, with the result that the bacterial counts dropped to a few per cubic centimeter.

A seventh hazardous procedure dealt with multiple formula rooms. A revolutionary change in social custom concerning childbirth occurred especially during the 1930's. The number of hospital deliveries increased by several hundred per cent. With increasing numbers of deliveries, the hospital increased the number of wards, and strange to relate, there was a corresponding increase in the number of formula rooms. These multiple rooms with their lack of good aseptic and sterilizing procedures, the use of nurses in training with no set standard of bacteriological technique, and a changing personnel, led to high bacterial counts and a multiplying possibility of toxicosis or infection by indirect contact through food. By consolidating these operations in a central laboratory in each hospital, there was not only greater economy but there was also established a uniformly high standard in procedure.

As an example of the above situation, and this was no exception, at one hospital there were 598 deliveries in 1930 and 2,028 in 1940. With this increasing number of deliveries and wards, the number of formula rooms was increased to three. During that period there were three separate outbreaks of diarrhea. By 1940 there was established a single formula room operated under a standard aseptic procedure. Since that time the day-old formulae have been practically sterile and despite the 4,028 deliveries in 1947, the nurseries have been free from epidemic diarrhea and impetigo. In a general way the above applies to the other six supervised hospitals.

STANDARD FORMULA ROOM PROCEDURES

The following procedure for preparing formula may be designated "The Chilled Method of Preparing Formula":

1. Autoclave all equipment, including all the nipples. Protect nipples from contact with container by wrapping in toweling.

2. Autoclave formula stock water, cool to room temperature, and chill overnight in refrigerator.

3. Record temperature of refrigerator at 9 A.M. and 1 P.M. Temperature should be set at 40° to 45° F. and at no time should go above 50° F.

4. It is desirable that the formula nurse should not be required to prepare the bottled food by more than three different formulae.

5. Practice good bacteriological laboratory technique in preparing and bottling the food. And at least once a week culture six to ten 24-hour formulae to check the effectiveness of the aseptic procedures and refrigeration.

6. Experience indicates that bacterial counts of 24-hour formulae should not be more than 500 per cubic centimeter and no single count should be more than 10,000. Good procedure gives counts of less than 5. Counts over 100,000 are a danger signal indicating errors in aseptic or mechanical procedures. Counts of 1,000,000 or over point to a possible outbreak of infant diarrhea.

A recent procedure for rendering the formulae safe for infants is that of autoclaving the bottled food, after having been nippled and capped, by the high pressure—low temperature method. This autoclave equipment is now on the market. It is used in two local hospitals, and in over 500 samples of formulae so prepared over 99 per cent were sterile.

CONCLUSIONS

1. In either large or small hospitals, any one of the several technical errors here related may lead to a serious epidemic.

2. If errors are eliminated and the day-old formulae are practically sterile, there is no danger of an explosive, fatal, foodborne outbreak.

3. If the formulae are aseptically prepared, any infection introduced into the nursery may be spread by contact, but these cases will be mild and of low virulence.

4. The formula room procedure should be checked weekly by bacteriologic examination of day-old food.

BOTULISM AND TICK PARALYSIS

In the Differential Diagnosis of Acute Bulbar Poliomyelitis

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POLIOMYELITIS occurs throughout the United States at the present time in endemic proportions throughout the year, and increases to epidemic incidence in certain localities in the middle and late summer months. The bulbar type of this disease is seen usually in isolated cases, but again in certain epidemics this type has been predominate. Bulbar poliomyelitis, as the name implies, is reserved for that type of the disease in which the cranial nerves arising from the medulla oblongata and pons are involved. It is, however, loosely applied to any case of poliomyelitis in which there is cranial nerve involvement.

In the last twelve-month period two cases of clinically diagnosed bulbar poliomyelitis which have been referred to this hospital for diagnosis and treatment have been extremely interesting and are worthy of reporting.

CASE REPORTS

Case 1.—G. B., a 10-year-old white girl, entered Doernbecher Hospital Nov. 15, 1947. The child was referred here from Redmond, Ore., as a bulbar poliomyelitis patient with the complaints of double vision, difficult breathing, flaccid neck and extremities, stomach-ache, and vomiting.

Family History.—The family, consisting of the father, the patient, and two younger siblings, lived with a rancher and his wife. They ate at a common table and used home-canned foods. The father could not recall any foods eaten Nov. 13, 1947, except hamburger and potatoes. No other members of the family group were ill; however, the father stated he could not get his eyes to focus, and that he saw double that evening. The city physician was called and agreed to examine the father at that time.

Present Illness.—Upon arising on the morning of Nov. 14, 1947, the patient complained of seeing double and shortly thereafter complained of abdominal pain. She ate a light breakfast and returned to bed as she did not feel well. She vomited at 10 A.M. and again at 1 P.M. and became progressively weaker and flaccid. That evening she continued to vomit, was unable to swallow, and was unable to move herself voluntarily. She was incontinent of urine and choked on mucous accumulations in the pharynx during the night. She was taken to a physician the following morning; he did a lumbar puncture and arranged to have the child sent here as a bulbar poliomyelitis patient. She was transported 250 miles by ambulance to this hospital, receiving oxygen by nasal catheter en route. She arrived here on the evening of November 15, having been entirely without fluids for the previous twenty-four hours.

Physical Examination on Entry.—Examination revealed a dehydrated, slender, 10-year-old white girl with a flaccid paralysis of all extremities, back, and neck. She was unable to talk or swallow, although she could whisper

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very faintly and with great effort. Her color was ashen. She complained of no pain. Temperature was 97° F., blood pressure 155/105, respiration 30 and very shallow. The patient was fully conscious, and would blink, and attempt to whisper replies. The upper eyelids could only be raised about halfway. The conjunctiva were injected and there was a slow, lateral nystagmus present. The pupils were 3 mm. round and equal, and did not react to light or accommodation. Funduscopic examination was negative. Expression was limited to a faint grimace and smile. The mucous membranes of the mouth and pharynx were dry, and the pharynx was filled with thick, tenacious mucus. The tongue could not be moved, and the gag reflex was absent. The diaphragm was high, and respirations were shallow, regular, and entirely intercostal in type. Examination of the chest and abdomen was otherwise negative. The extremities were symmetrical, very slender, and entirely flaccid. They could not be moved against gravity but were moved feebly on command. The patient could be flexed into any position with ease. Reflexes were entirely absent. Kernig and Brudzinski were negative. The genitalia were normal except that the vaginal introitus was gaping. Rectal tone was decreased and two fingers were inserted into the rectum without resistance. Sensory examination could not be evaluated.

Laboratory Examination.—Spinal fluid was clear, Pandy negative, pressure would not register on the manometer, and the cell count was 3 lymphocytes. White blood count 28,150 with differential of 69 per cent neutrophiles, 12 per cent staff cells, 17 per cent lymphocytes, and 1 per cent monocytes. Blood sugar was 90 mg. Alkali reserve was 62 volumes per cent. Blood culture was negative.

Hospital Course.—The patient was placed in Trendelenburg position, parenteral fluids and nasal oxygen were started. At 6:30 A.M., Nov. 16, 1947, respirations ceased; she was maintained with artificial respiration until transferred into a respirator. That afternoon a tracheotomy was performed with the patient in the respiratory. The patient was still conscious and would reply to questions by blinking her eyes twice for "yes" and once for "no." Large quantities of mucus were aspirated from the trachea, and she would develop sudden respiratory embarrassment with cyanosis. Bronchoscopy through the the tracheotomy opening was done frequently, averaging twice a day for the first two to three weeks. Large crusts, which often completely occluded one of the main-stem bronchi, were removed with foreign-body forceps. The patient remained in the respiratory for seventy-one days. A brief résumé of this course will be presented.

By Nov. 21, 1947, the patient had become less responsive; it was noted that on bronchoscopy exudate was presenting itself into the upper portion of the right main-stem bronchus, and it was felt that she had developed a right upper lobe pneumonia. Word was received that day that the father had expired at the city isolation hospital of an acute bulbar paralysis.

By Nov. 23, 1947, facial expression had gradually failed and the patient could not open her eyes, blink, or smile. The pupils were dilated and did not react to light. The patient was maintained on intravenous and subcutaneous fluids in addition to tube feedings and prophylactic penicillin. Pathologic report reveals that the diagnosis of poliomyelitis could not be substantiated as the cause of death in the father. It was decided at this time that the child should be given Botulinus antitoxin. The antitoxin was obtained on November 27 and three injections of 10,000 units each of Anti A and B Botulinus antitoxin were given at four-hour intervals. Following the last injection the patient developed a generalized urticarial rash and angioneurotic edema of

the face. This reaction responded to adrenalin but further administration of antitoxin was not felt justified. On November 28 it was demonstrated that the patient had a bilateral sixth nerve paralysis. On December 1 facial expression was returning and she was able to move the extremities to a slight degree. The patient was able to swallow liquids without the Levine tube on Jan. 12, 1948. For the first time the patient was able to remain out of the respirator on Jan. 17. She remained out with encouragement for forty minutes. Two days later she remained out for forty-eight hours. She was gradually completely removed from the respirator in the following week. She could not cough up secretions and tracheotomy was maintained for aspiration. She was exercised daily in the Hubbard tank, and regained strength and weight rapidly. The tracheotomy tube was removed Feb. 10, 1948, having been in place for eighty-five days. The wound closed in four days. She was discharged from the hospital February 17, at which time she still had practically complete loss of movement of both leaves of the diaphragm, and complete loss of accommodation. She was fitted with glasses for near vision.

The Public Health Service reported demonstrating botulinus organisms from the scrapings recovered from the dishes used by this family group on November 13.

No report has been found in the literature of a patient with botulism who has survived after having developed a complete pharyngeal paralysis. Certainly this patient would have succumbed if it had not been for the respirator, tracheotomy, and constant nursing and medical attention.

Correspondence with the patient nine months following her recovery reveals she is well, rides a bicycle, participates in games, and uses her glasses only for reading.

CASE 2.—R. G., a 5-year-old white girl, entered Doernbecher Hospital July 19, 1948, with a complaint of paralysis. Family history was noncontributory.

Present Illness.—July 15, 1948, the mother noticed the child persistently stumbled when she walked, and the following day she was unable to walk except by holding on to objects. On July 17 she had difficulty in swallowing and complained that her throat hurt. The following day she was unable to walk, talk, or hold her head up. She had no respiratory difficulty and did not complain of pain. She was examined by a physicain and referred into Doernbecher Hospital as a bulbar poliomyelitis patient. Physical examination on entry revealed a well-developed, well-nourished white girl who was flaccid in all extremities, back, and neck. She could not move her head and could not talk. Temperature was 99.6° F. (R), blood pressure 108/72. Respirations were rapid, irregular, and predominantly diaphragmatic. The skin was pale and dry, the mucous membranes were dry. She was unable to swallow fluids and the gag reflex was absent. The chest and abdomen were negative. Extremities were completely flaccid with loss of all reflexes.

Laboratory Examination.—Spinal fluid was clear, Pandy negative, cell count 8, total protein 20 mg. per cent, culture negative. White blood count was 28,000 with differential neutrophiles 57 per cent; eosinophiles 2 per cent; lymphocytes 11 per cent; monocytes 1 per cent; basophiles 1 per cent; staff cells 28 per cent; sedimentation rate 2/10; serology negative.

This case was presented briefly on morning rounds, July 20, 1948, as an atypical poliomyelitis patient with bulbospinal involvement manifesting flaccidity, negative spinal fluid, leucocytosis, and no temperature elevation. With a strong recollection of Case 1 in this paper, the parents were again contacted

and questioned, particularly as to the type of food recently eaten and health of the remainder of the family group. This interrogation was negative and the patient was re-examined. Findings at that time were essentially as recorded on entry; however, respirations were more impaired and the patient was showing mild cyanosis. A careful search was made for a tick, and the latter was found lying under a thick mass of hair over the left parietal area. On closer examination the tick was engorged, measuring 10 mm. in length, 7 mm. in transverse diameter, and 3 mm. in depth. An area of scalp with a radius of 2 cm. about the attachment of the tick was covered with fecal material which had the appearance of coarse pepper. The tick was removed by an elliptical incision of the scalp removing the area of attachment of the tick.

Hospital Course.—On the following morning, July 21, the patient was definitely improved, color was good, limbs were moved voluntarily, and she was taking oral fluids. On July 23 the patient was sitting up in bed, talking, and eating well. She was extremely uncooperative, and physical examinations could not be too well evaluated. The white blood count had dropped to 11,000. The patient was walking on July 24, afebrile and entirely recovered. She was discharged that day.

The tick in this case was *Dermacentor variabilis*, or the dog tick.

SUMMARY

1. Two patients manifesting bulbar paralysis are presented, each of which have been initially considered to have poliomyelitis.

2. These two cases demonstrate the necessity of summarization of all laboratory, clinical findings, and, if these are not in agreement with the diagnosis of poliomyelitis, further search is indicated.

ROENTGEN MANIFESTATIONS OF INFANTILE HYPERTROPHIC PYLORIC STENOSIS

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INTRODUCTION

DESPITE the prominent role of radiology in the recognition of gastrointestinal disorders, comparatively few pediatricians, surgeons, and radiologists fully appreciate the value of roentgen methods in the diagnosis of infantile hypertrophic pyloric stenosis. This may be explained by the fact that certain roentgen criteria proposed many years ago have been found unreliable for this condition.[1, 2] Also, there are many clinicians who are hesitant to utilize the procedure in infants for fear of possible harmful effects.[3, 4]

The purpose of the following study is twofold. First, newer, more specific roentgen signs are emphasized and their value determined in an unselected series of cases in the manifest stage of infantile hypertrophic pyloric stenosis. Second, information as to the presence of residual pyloric changes was obtained by roentgenologic follow-up studies ranging from five months to twenty-two years after successful surgical treatment by the Fredet-Ramstedt operation.

CLINICAL CONSIDERATIONS

The clinical features of hypertrophic pyloric stenosis have been adequately described in many excellent reports and will not be elaborated upon here.[5] It may suffice to state that palpation of the pyloric tumor is generally considered to be the most important clinical sign. Though experienced observers have claimed that this may be possible in practically all cases,[1, 6] other qualified clinicians have been unable to demonstrate a palpable mass in more than two-thirds of cases.[4, 7] It has been our observation that in some instances competent physicians were at variance in their opinion as to the presence or absence of a tumor. Also cases have been reported in which a mass was thought to be present clinically, but in which a normal pylorus was subsequently demonstrated at operation.[4] The occurrence of these cases makes it desirable to utilize methods which may improve the accuracy of clinical diagnosis.

ROENTGENOLOGIC CONSIDERATIONS

Earlier roentgen studies of hypertrophic pyloric stenosis placed much emphasis on such signs as gastric hyperperistalsis, dilatation, and retention as important features in the establishment of a correct diagnosis.[8, 9] These signs cannot be considered as specific since any of them have been found to occur

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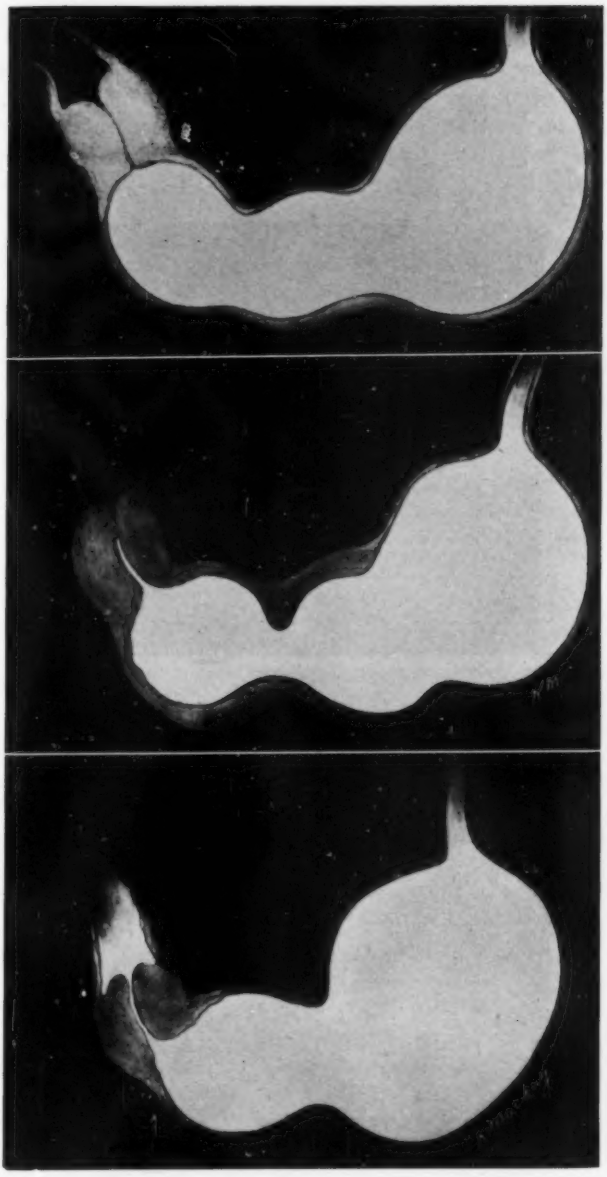

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1.—The pathologic changes of hypertrophic pyloric stenosis. Marked obstruction prevents filling of the pyloric channel.

Fig. 2.—A small amount of barium has entered the narrowed pyloric channel, the "string sign."

Fig. 3.—The pyloric tumor encroaches upon the lumen of the pyloric channel and protrudes into the base of the duodenal cap.

in such conditions as gaseous distention of the intestines,[10] severe infection, cerebral trauma, and duodenal atresia.

The modern criteria for the radiologic diagnosis of infantile hypertrophic pyloric stenosis were introduced by Meuwissen and Slooff in 1932.[11] Subsequent articles in the European and American literature have served to corroborate their findings.[12, 13] In all these studies an attempt was made to demonstrate the radiologic equivalent of the underlying anatomic changes.

Fig. 4.—Typical "string sign."

It will be remembered that the pathology of this condition consists of a hypertrophy of the pyloric muscle which enlarges to involve not only the true pylorus but also the prepyloric segment of the stomach, the so-called "canalis egestorius." Mucosal thickening further diminishes the caliber of the lumen. These anatomic changes result in the formation of a narrow canal at the junction of the stomach and duodenum. The direct demonstration by barium studies of this narrowed segment forms the basis of current x-ray diagnosis. On proper filling the stenotic canal will be outlined by a thin streak of barium measuring usually 2 to 3 cm. in length. This radiologic pattern is commonly referred to as the "string sign" (Figs. 2 and 4). To our knowledge, this radiologic sign has not been observed in any other gastric lesion of infancy and should be considered as pathognomonic. In markedly obstructed cases it may be difficult to demonstrate the stenotic canal, but by proper manual compression its most proximal portion can frequently be visualized at the height of a peristaltic wave. A short streak of barium, having the contour of a bird's bill, may then protrude from the distal part of the pyloric antrum, the so-called "pyloric beak" (Fig. 5).

A second valuable radiologic sign is the indentation of the base of the duodenal cap (Figs. 3 and 6). The structural basis for this feature is the cervixlike protrusion of the pyloric tumor into the lumen of the proximal

duodenum. Contrary to the findings of Miller and Ostrum[10] that changes in the duodenal cap were not observed by them, we have found indentation of the base of the duodenal cap to be of appreciable value.

Fig. 5.—A minimal amount of barium has penetrated into the proximal portion of the pyloric channel, the "pyloric beak."

Fig. 6.—*S*, String sign; *I*, Indentation of proximal duodenum.

TECHNIQUE OF ROENTGEN EXAMINATION

Previous writers have expressed fear as to the effects of the oral administration of barium in these infants.[2, 3] It has been stated that barium might impact in the pylorus, completing the obstruction, or that barium might be aspirated into the lungs. In our experience the procedure has been found to be entirely harmless.

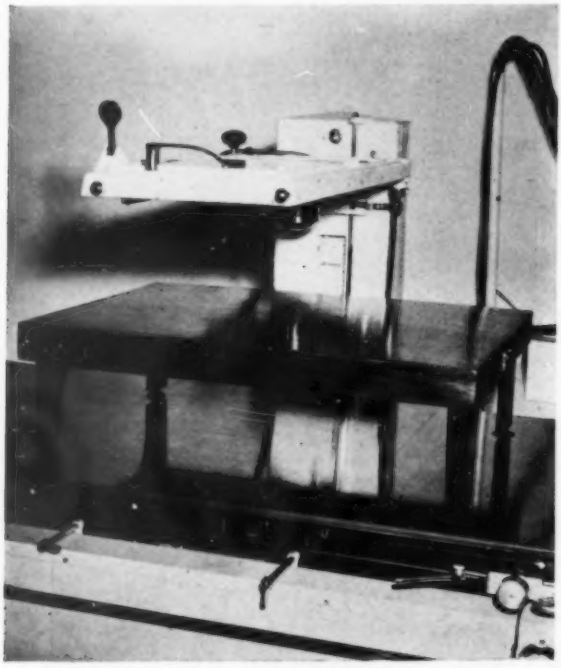

Fig. 7.—Collapsible elevating board utilized in fluoroscopy of infants.

The use of a stomach tube has simplified the examination considerably. After withholding food for a few hours, a sterile gavage tube is inserted into the stomach under fluoroscopic control. Structural changes in the esophagus may be detected by difficulty in the passage of the tube. Any retained fluid and air are aspiration from the stomach and approximately 1 to 2 ounces of a thin barium mixture is instilled. After the completion of the examination residual barium may be withdrawn. It is very important to examine the infant in the oblique and lateral positions in order to visualize properly the pyloric channel. Spot films taken during fluoroscopic examination are used extensively to record fluoroscopic impressions. In our studies we thought it advisable to use a collapsible 7-inch elevating board, placed on the x-ray table top (Fig. 7). The increased tube-to-patient distance serves two purposes. The sharpness of the image of spot roentgenograms is improved, and at the same time the radiation exposure of the patient is reduced.

RESULTS

A. Preoperative Studies.—The results of our findings in patients examined during the manifest stage of the disease are recorded in Table I. In nineteen out of twenty-two cases positive roentgen evidence was obtained. All these cases were proved by operation except for one which was treated medically. In the total of nineteen positive cases, all showed the "string sign" and seven showed, as an additional finding, an indentation of the base of the duodenal cap.

TABLE I. X-RAY STUDIES DURING MANIFEST STAGE OF DISEASE

NO.	NAME	RACE	SEX	SURGICAL PROOF	PALPABLE MASS	X-RAY SIGNS	
						STRING SIGN	INDENTATION OF CAP
1	P. C.	W	F	+	0	+	0
2	C. S.	W	M	+	0	+	0
3	P. R.	W	M	+	+	+	0
4	H. G.	W	M	+	+	+	0
5	J. M.	W	F	+	0	+	+
6	J. B.	W	M	+	0	+	0
7	J. J.	W	M	+	+	+	+
8	B. B.	W	M	+	+	0	0
9	McK.	W	M	+	+	+	0
10	L.	W	M	Not operated on	+	+	+
11	L.	W	M	+	+	+	0
12	M. C.	N	F	+	+	+	0
13	W. P.	N	F	+	0	+	+
14	C. M.	N	F	+	0	+	0
15	J. C.	N	M	+	0	+	0
16	J. M.	N	M	+	0	+	+
17	F. S.	N	M	+	0	0	0
18	W. B.	N	M	+	+	0	0
19	E. S.	N	M	+	0	+	+
20	E. W.	N	M	+	+	+	0
21	W. H.	N	M	+	+	+	0
22	R. M.	N	M	+	0	+	+

In the remaining three cases the severity of the obstruction prevented filling of the narrowed pyloric channel, so that a specific diagnosis could not be made (Fig. 1). It is conceivable that administration of antispasmodics might have facilitated visualization of the involved gastric segment.

With proper attention to the pathognomonic features of infantile hypertrophic stenosis, the radiologist may improve his accuracy. During the past five years our radiological service has studied more thoroughly the characteristic features of this disease and has demonstrated the specific radiologic signs with increasing frequency. Concurrently the clinicians have placed greater confidence in roentgen diagnosis and have referred practically all suspected cases for study.

An interesting sidelight of our small series of twenty unselected cases at Grady Memorial Hospital in the past four years is the high incidence of the disease in the Negro race (eleven Negro, nine white). Many earlier reports on this subject stress the rarity of this condition in the Negro race.[14] Our observations tend to confirm the findings of McGahee,[15] who noted that infantile hypertrophic stenosis occurred not infrequently among Negro infants.

B. Follow-up Studies.—In sixteen cases follow-up gastrointestinal examinations were performed at intervals of from five months to twenty-two years following successful treatment by operation. The findings of these studies are summarized in Table II. In all but one case (No. 8, aged 1½ years) persistent changes in the most distal portion of the stomach were observed, consisting of varying degrees of narrowing as well as diminished or absent peristalsis (Figs. 8, 9, 10, 11). Several of these patients demonstrated basilar indentation of the duodenal cap. Similar findings were observed in one patient treated medically when examined five months after clinical recovery. We were impressed that despite the radiologic changes proper gastric emptying was a regular occurrence in all these cases. Similar studies were previously undertaken by Runstrom[16] and also Andresen,[13] who noted that a pyloric deformity may persist for many

Fig. 8.

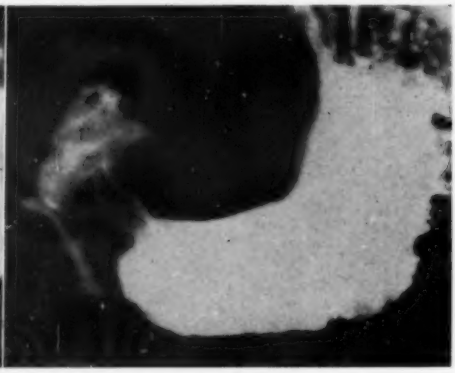

Fig. 9.

Fig. 8.—Hypertrophic pyloric stenosis five months following Fredet-Ramstedt procedure. Note marked narrowing of pyloric channel and indentation of duodenal cap.

Fig. 9.—Case 5, four years following surgery. Note residual distortion of pyloric channel with reappearance of mucosal folds.

TABLE II. FOLLOW-UP FINDINGS

NO.	NAME	RACE	SEX	LENGTH OF FOLLOW-UP INTERVAL	POSITIVE FINDINGS
1	I. H.	W	M	22 years	+
2	V. M.	W	M	13 years	+
3	C.	W	M	10 years	+
4	D. C.	W	M	6 years	+
5	W. P.	N	F	4 years	+
6	W. B.	N	M	3½ years	+
7	P. C.	W	F	2½ years	+
8	F. S.	N	M	16 months	0
9	H. G.	W	M	13 months	+
10	C. S.	W	M	10 months	+
11	P. R.	W	M	10 months	+
12	E. S.	N	M	7 months	+
13	E. St.	W	M	6 months	+
14	C. M.	N	F	6 months	+
15	E. W.	N	M	5 months	+
16	W. H.	N	M	5 months	+

Fig. 10.—Case 3, ten years following operation. Residual narrowing of pyloric segment.

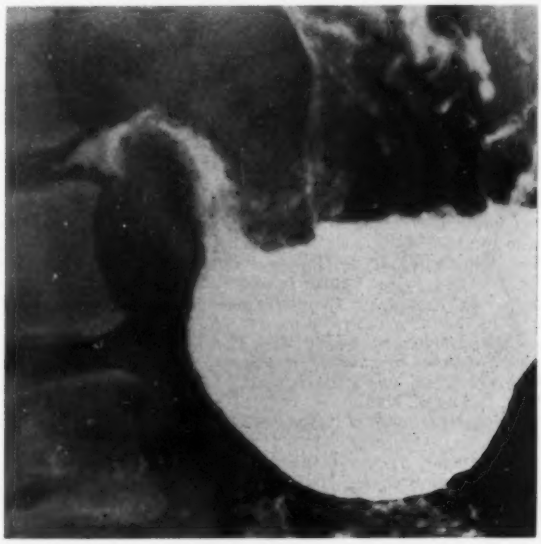

Fig. 11.—Case 1, twenty-two years after successful surgical treatment.

years. These radiologic observations suggest that there are, following operative procedures, residual changes in tone or structure at the site of the hypertrophic pyloric stenosis.

These residual changes are of importance to the roentgenologist who occasionally encounters adolescent or adult patients with narrowing or stiffening of the prepyloric or pyloric portion of the stomach. Conceivably, some of these patients may have had hypertrophic pyloric stenosis in infancy.

SUMMARY AND CONCLUSIONS

The roentgen criteria of infantile hypertrophic pyloric stenosis are briefly enumerated and a technique of radiologic examination is described.

Roentgen observations of an unselected series of cases in the active stage of infantile hypertrophic pyloric stenosis revealed positive signs in nineteen out of twenty-two cases. These changes consisted of (a) narrowing and stiffening of the stenotic canal in the pyloric tumor ("string sign," "pyloric beak") and (b) indentation of the base of the duodenal cap. These specific signs occur in association with other nonspecific signs such as delayed emptying, gastric hyperperistalsis, and dilatation.

In fifteen out of sixteen cases examined after complete recovery following a Fredet-Ramstedt operation, residual pyloric deformity was observed consisting of varying degrees of narrowing and diminished or absent peristalsis. Generally the postoperative x-ray changes were less pronounced than those seen during the manifest stage of the disease. In one patient distortion of the pyloric segment of the stomach was still present twenty-two years following operation. In spite of these radiologic changes, gastric emptying was entirely normal.

Though in the majority of cases of infantile hypertrophic stenosis the diagnosis may be established on the basis of the clinical studies, there remain many cases in which x-ray examination will materially assist in the establishment of a correct diagnosis.

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PRECOCIOUS PUBERTY

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THE cases presented herewith emphasize what has been expressed by several others, and particularly stressed by Novak, that, except for the relatively rare instance, precocious puberty in the female is just what the name would imply, i.e., the development of pubertal changes at an earlier time than usual, these changes being based upon the same physiologic processes in the various endocrine glands as are at work during puberty which occurs at the usual time.

In the past the belief has been rather general that when evidences of sexual maturity occurred in girls at an early age, certainly below the age of 8 years, such changes were caused by a tumor of one of the endocrine glands, notably a granulosa cell tumor of the ovary. Thus Crossen[1] states, "for genuine menstruation to take place, there must be considerable development of the genital organs, and this very rarely occurs before the age of ten, except in a patient with granulosa cell tumor."

In virtually all of the textbooks the discussion of precocious puberty begins with a description of pathologic conditions, usually neoplastic, which may exist in one or another of the various endocrine glands, or pathology involving certain portions of the brain, particularly the hypothalamus and floor of the third ventricle, which results in premature changes in the sexual and secondary sexual characteristics of the individual. Reference to those cases of premature sexual development which occur in the absence of any demonstrable pathology, either in the endocrine system or elsewhere, is usually relegated to a short paragraph at the end of the chapter, if mentioned at all.

It is not the purpose of this paper to discuss in any detail the pathologic processes which may occur in the endocrine system, or lesions involving the brain which give rise to premature sexual development changes as part of their manifestations. These have been exhaustively treated within the limits of our present knowledge in other sources. However, a few observations are pertinent.

Almost without exception, in cases of premature sexual development dependent upon pathology involving the endocrine system, such as benign or malignant tumors of the pineal gland or the adrenals or lesions involving portions of the brain, particularly the region of the hypothalamus, other systems are involved, sometimes widely and markedly. This is far from consistent with the evident normality of the pubertal changes which occur in the type of case under discussion. Thus tumors involving the pineal gland cause isosexual changes, but they are almost exclusive in the male. Neoplasms of the adrenals are almost invariably masculinizing in the female, marked by hypertrophy of the clitoris and hirsutism especially, and pathology of the hypophysis and regions of the

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brain mentioned above involve manifestations of which the sexual or secondary sexual are only a part.

According to Novak,[2] there is no recorded instance of a tumor of the pituitary being the cause of precocious pubertal changes. This is remarkable, considering the fundamental position held by the pituitary in female sexual maturity, and its maintainance after the menarche. Novak also states that of 60,000 gynecologic admissions to the Johns Hopkins Hospital over a period of sixty years, only one case of granulosa cell tumor of the ovary as a cause of precocious puberty was recorded.

In the type of case represented by the four histories which appear below, no pathology, neoplastic or other, was found at the time the patient was first seen, or after, to account for the early onset of pubertal changes. These changes were entirely normal except for the time at which they appeared. The progress of these changes after their appearance was also entirely normal. Novak and others have called cases such as these "precocious puberty of constitutional type." I am in agreement with Novak that cases falling into this class are in the great majority rather than the minority, as it has been the tendency to believe.

In this type, the bone changes also are consistent with normal puberty. Most of these little girls are, from a general standpoint, more mature than others of the same chronological age. In my experience their mental development is advanced. This last is at variance with other recorded observations regarding the mental development of these patients. Thus Novak[3] has previously stated that "the mental development of the patient has been described as very defective, almost all authors speaking of the childish type of mind seen in these patients. For example, Lenz's patient still played with dolls and very small children at the age of 10 years." Of the four patients in my own experience, one was developed at least to her chronological age, and the other three were definitely beyond in comprehension, use of words, personality traits, etc.

Stimulation of bone growth which is normal for puberty is also found in these cases, except that epiphyseal closure is accelerated. Consequently, in the cases which I have observed these little girls were developed beyond their chronological age when first seen and for a time after, but they are all destined to be below the average in height because of early epiphyseal closure.

Novak, in an excellent article which appeared in the January, 1944, issue of the *American Journal of Obstetrics and Gynecology*, cites nine cases of precocious puberty, all of which fell into the group under discussion. Laparotomy was done in six cases, and in none was any neoplastic disease of the ovaries found. In three of these corpora lutea were found, further attesting to the normality of the pubertal changes which had been previously noted. In all cases ovarian enlargement, when found, was due to simple cysts of various kinds. In the four cases presented below, laparotomy was done in two. In one case a definite enlargement of the ovary was found preoperatively, which proved to be a lutein cyst, and multiple small follicle cysts were found in the other. In neither was there any evidence of neoplasm in the ovaries or elsewhere.

In theorizing upon the factor or factors which set in motion sexual maturity at an abnormally early age, the presence of certain genic factors in the chromo-

somes of a recessive character has been postulated,[2, 4] which factors act in conjunction with the endocrine system to "pull the trigger" as Novak puts it, at a time earlier than usual, the changes themselves being within normal limits of puberty. At least in the light of our present knowledge such a postulation seems reasonable.

If one were precise in the use of words, no other designation than precocious puberty would be needed for these cases since the name means nothing except puberty occurring earlier than its usual time. In the various pathologic conditions causing certain changes in the genitalia and secondary sexual characteristics, the diagnosis ought to be simply that of the pathologic process present, recognizing the sexual changes merely as one manifestation of the whole picture. To do otherwise, as we are wont to do with precocious puberty, is equal to having our main interest and attention centered upon the bronzing of the skin in Addison's disease.

An insufficient number of these cases of precocious puberty have been followed for a long enough time to know what happens to all or most of them later, such as the age of their menopause or their fertility. If one accepts the fundamentally physiologic nature of these patients, there is no reason to suppose that they would be different from other women in these respects. Novak[2] recites a case reported by Haller, in which menstruation began at 2½ years, with the menopause at the age of 52. A patient reported by Robbelin was still menstruating at the age of 32½ years. The normality of the sexual maturity process in several of these little girls has been further attested by pregnancies which have occurred at an early age.

These patients should be expertly examined, preferably under anesthesia. It is my opinion that laparotomy is not indicated unless palpable evidence is found to indicate it. One is impressed in these cases by the orderliness of normality of the sexual development and the usual absence of evidences of pathology in the pelvis or elsewhere. In the absence of diagnosable pathology, the treatment of these patients consists in psychotherapy—some of it for the patient, but most of it for the mother and the family.

CASE 1.—B. F. was first seen at the age of 4½ years. Breast development had been noticed at the age of 4 years. There had been no bleeding. The patient appeared beyond her years in general physical and personality development. The breasts were markedly developed. There was a thick, fine down over the pubes and labia, but no axillary hair, and the clitoris was not hypertrophied. General physical examination was negative. Numerous examinations of the pelvis were made, two under anesthesia. No palpable pathology was ever found. Operation was not done. The patient is now 10 years of age, and she has been menstruating regularly and normally since the age of 7 years. The epiphyses at the age of 9 years were practically closed. Her present height is 5 feet.

CASE 2.—N. J. was first seen at the age of 7 years. Enlargement of the breasts had begun at the age of 5 years, and had been progressive. Physical and mental development appeared beyond her chronological age. The breasts were well developed, with large, pigmented areolae. There was a considerable amount of long, black, pubic hair. There was no axillary hair. The genitalia had the characteristics of late puberty. Pelvic examination was made several

times, once under anesthesia. There was never any palpable pathology. The first menstrual period occurred at the age of 7 years, and has been regular and normal since. She is now 9 years of age.

Fig. 1.

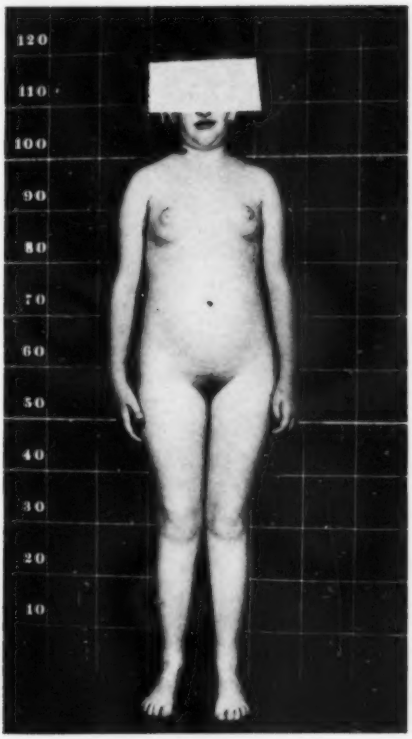

Fig. 2.

Fig. 1.—Case 1. Photograph at age of 8½ years. Breast development began at 4 years. Menstruation began at 7 years.

Fig. 2.—Case 2. Photograph at age of 7 years. Breast development began at 5 years. Menstruation began at 7 years.

CASE 3.—E. B. was first seen at the age of 8 years. Her breasts were markedly developed before the age of 6 years. Menstruation had begun at 7½ years, and had been fairly regular and otherwise normal since onset. Physical and mental development appeared beyond her chronological age. Examination revealed a girl who might have been 14 years old. The genitalia were adult in appearance. There was a dense growth of pubic and axillary hair. Pelvic examination disclosed a mass in the right lower pelvis which seemed to be an ovary about 6 cm. in diameter. The uterocervical ratio was roughly 2:1.

Laparotomy was done, and the right ovary removed. The enlargement proved to be a lutein cyst, with many normal follicles in various stages of maturity.

There has been no regression in any of the patient's adult characteristics since the operation, and menstruation has occurred regularly and normally since.

X-ray studies were made in all of the above cases. No intracranial pathology was found. Advancement of the bone age was found in all cases, as shown in the accompanying illustrations.

Fig. 3.—Case 3. Photograph at age of 8 years. Breast development began at 5 years. Menstruation began at 7½ years.

CASE 4.—E. M. Patient was admitted to Children's Hospital in Denver in 1942, at the age of 4 years. She had gained from 35 to 57 pounds during the previous year. During the four months previous to her admission to the hospital, she had been nervous and irritable, which was ascribed to the rather large amounts of thyroid which she had been receiving. Breast enlargement had been noticed at the age of 3½ years. There had been no bleeding. Examination revealed a girl somewhat average height for her age, and overweight. The breasts were moderately enlarged. Areolae were distinct. There was moderate enlargement of the genitalia but the clitoris was not hypertrophied. There was no pubic or axillary hair. Vaginal smears showed squamous cells which were of the adult vaginal type. Roentgenograms were made at this time of the skull and upper extremities. The sella turcica was normal. Examination of the wrists showed advancement of the bone age, there being seven of the eight carpal

bones present (normal for age 4 or 5). There was considerable development of the radial epiphyses in advance of that considered normal.

Exploratory laparotomy was done for possible granulosa cell tumor of the ovary as a cause of the precocious sexual development. The ovaries were about 2 by 1 cm. in size and contained multiple cysts. Section of the left ovary was removed for pathologic examination. Kidney regions were palpated and no abnormalities were found.

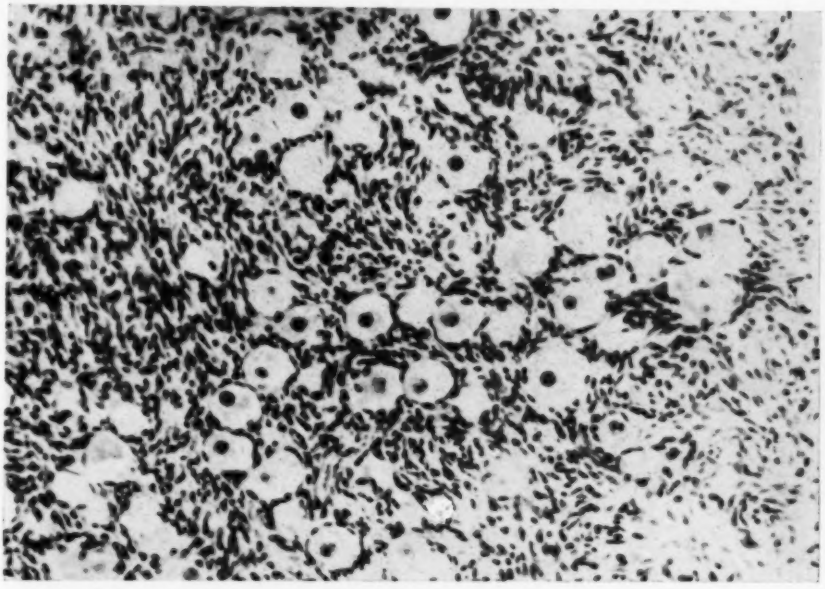

Fig. 4.—Case 4. Sections of ovary removed at age of 4½ years, showing normal follicles.

Microscopic Examination.—"The sections include the cortex and a portion of the medulla of the ovary. The cortex shows normal anatomical relationships and contains many primordial follicles. Several portions of follicle cysts are included in the sections. These are of the atretic follicle type, with a prominent theca interna layer. One of them contains fresh hemorrhage. Diagnosis: Follicle cysts of immature ovary."

This patient is of particular interest because she has been followed subsequently by her pediatrician, Dr. John M. Nelson, and also by the Child Research Council of the University of Colorado Medical Center. She is now 11 years of age. She began to menstruate at the age of 6, and her periods have been regular and normal to date.

The following examinations and reports were made by the Child Research Council when the patient was 9½ years of age:

X-ray Study.—"The bone to bone proportions are all well within average limits and present no peculiar relationships. Lengths are average except for lower leg bones which are somewhat above average for her age. Total body height (4 feet 8 inches) is similarly somewhat above average for her age. The disturbing element in this picture is the maturity of the skeleton. Many of the centers have already fused to shafts, especially at the elbow and ankle.

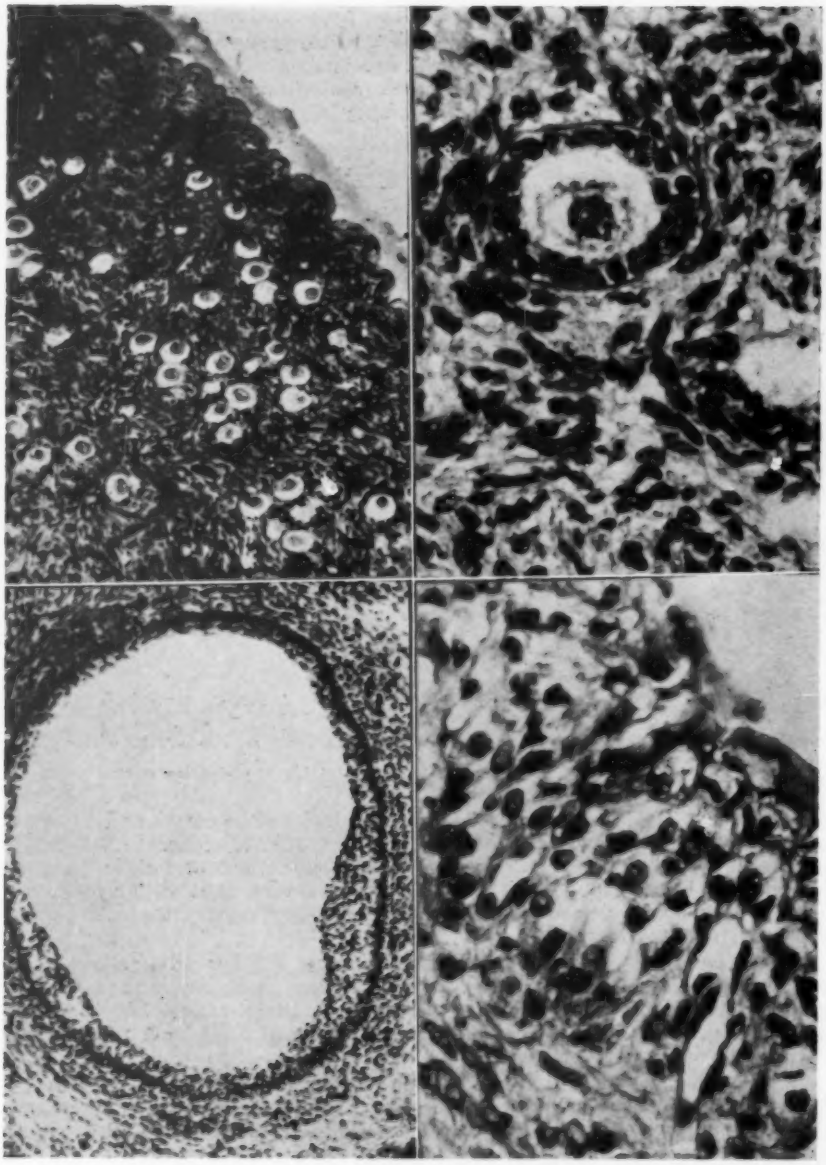

Fig. 5.—Case 3. Sections from right ovary: upper left, primordial follicles; upper right, follicle in early stage of development; lower left, fully developed follicle; lower right, lining membrane of the cyst.

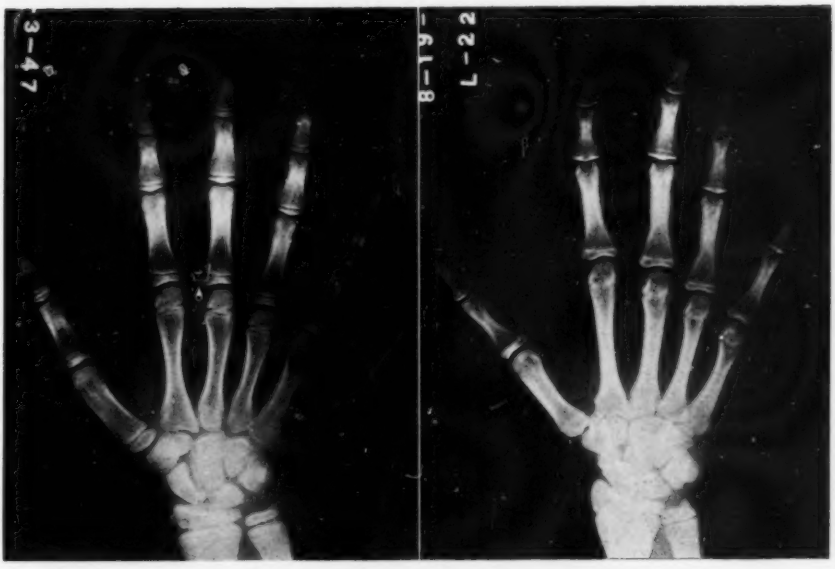

Fig. 6. Fig. 7.

Fig. 6.—Normal bone development in a girl of 9 years. Immature. Epiphyses open.
Fig. 7.—Case 1. Taken at age 9 years, showing advanced bone age.

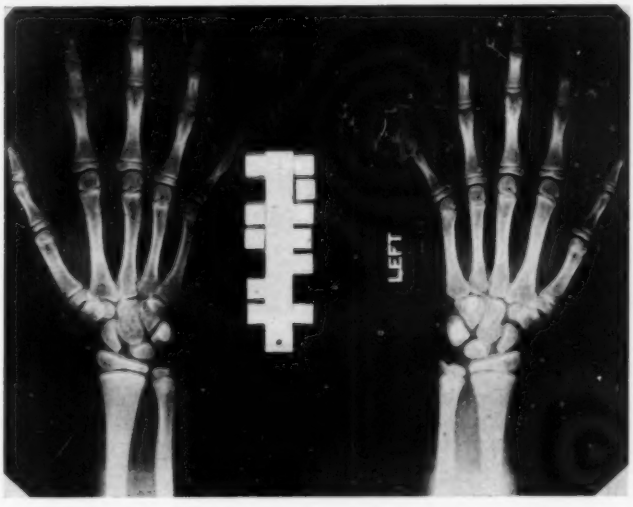

Fig. 8.—Case 2. Taken at age 7 years, showing advanced bone age.

The knee, shoulder, and hip epiphyses are almost fused and will probably close within 6 months. Thus the patient is at least four or five years accelerated over other girls her age. She cannot be expected to gain more than a possible inch in height from long bone growth. She may gain another two inches from the spine, but she is certainly destined to be a very short adult, probably under 5 feet. The skull pictures show a sella of normal size with normal density of the clinoids and floor.

Fig. 9.—Case 4. Taken at age 4½ years, showing advanced bone age.

"It would be interesting to know the time at which fusion of the epiphyses began. Usually one expects to see fusion of the capitellum to the humeral shaft shortly before the menarche. In this case, the patient's growth suggests that fusion has occurred more recently, probably within the past year." (Marion Maresh, M.D.)

Report From Psychiatrist.—"Patient has an I.Q. of 127. She appears to be functioning at a very superior level for her age and to have a mental age over two and one-half years above her chronological age. Vocabulary was on

the 14-year level. Reasoning, comprehension, and ability to express herself were all superior." (Cotter Hirshberg, M.D.)

Basal metabolic rate at this time was minus 10 per cent.

Fig. 10.—Also Case 4. Taken at age 9½ years, showing almost complete maturity of bones.

CONCLUSIONS

1. Except rarely, precocious puberty in the female appears to be what the name implies, viz., the onset and development of sexual maturity which is physiologic except for the time at which it begins.

2. This maturity involves not only the genitalia and secondary sex characteristics but the skeletal system as well. Because of the early closure of the epiphyses, these individuals are usually of short stature.

3. These patients should be expertly examined and a pelvic examination should be done under anesthesia. Surgery is not indicated unless palpable evidence is found to justify it.

4. Granulosa cell tumor of the ovary is rare as a cause of premature sexual development. Tumors of other endocrine glands, when accompanied by sexual change, are heterosexual in their manifestations. Lesions of certain brain areas, when accompanied by sexual changes, are also accompanied by other system changes which, in most cases, exceed those of the genitalia or secondary sex characteristics.

5. Treatment consists in psychotherapy directed to the patient, but particularly to the mother or family during the years which lie between the appear-

ance of sexual maturation and the time when these self-conscious little girls will merge with the group in their physical appearance, or, more correctly, when the group merges with them.

I wish to express my thanks to Dr. F. Craig Johnson of Denver, through whom Cases 2 and 3 were referred.

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A METHOD OF DETERMINATION OF SERUM pH APPLICABLE FOR CLINICAL USE

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DETERMINATION of the serum pH is of importance to the clinician since the carbon-dioxide combining power does not give accurate information concerning the acid-base balance in salicylate intoxication or in diseases associated with disturbances of respiration. Frequently it is difficult to decide from clinical and chemical evidence whether the patient is alkalotic or acidotic. In such a situation errors of pH 0.05 would be of no significance. A method which would fall within this range of error and would be applicable for clinical use would be of value. Methods of determining the serum or blood pH have not been of general clinical value because of technique required.[1] A trained technician, such as is not available in the average hospital, is necessary if precise results are to be obtained. If the determination is to be run at the bedside it is necessary to have the equipment and the technician available at all times. If the blood is to be sealed by the most exact methods, equipment is required which is not readily available and is expensive.

These studies were carried out because no data could be found in the literature concerning the effect of various factors on the serum pH determination when the blood was drawn under mineral oil. Since minor variations of pH do not invalidate its use in clinical medicine it was felt valuable to find out how long the blood could remain under oil and be centrifuged without significantly altering the determination. The technical errors inherent in this method are well understood, and it was surprising that the determinations were as constant as they turned out to be.

METHOD

A standard Beckman pH meter was used. The electrodes were 2.5 inch sealed glass and calomel electrodes. The open type electrode was used. Seven milliliter specimen vials were used for collection of the blood. Tight fitting tuberculin syringes with short beveled 22-gauge needles were found convenient for withdrawing the serum. Ordinary heavy mineral oil was used.

Blood was drawn under mineral oil in tight-fitting, dry syringes with precautions against the introduction of air into the syringe. Depending upon the hematocrit, 2 to 3 c.c. of blood were necessary. The sample was placed under 4 to 6 mm. of mineral oil in the vials and was centrifuged for five minutes at 2,500 r.p.m. After the pH meter was standardized, the serum was drawn into the tuberculin syringe slowly to prevent the introduction of air. Oil was cleaned from the needle, and the serum was introduced slowly into the cup with the tip of the needle against the bottom of the cup to prevent excessive contact

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with air. The determination was run immediately. Certain precautions had to be taken. The glassware had to be clean and dry. If the electrodes touched either the sides of the cup or each other the results were variable. The standardization of the meter and the determinations were carried out according to directions accompanying the instrument.

RESULTS

Studies were done to determine the effect of various factors on the determination. Blood was allowed to remain under oil for varying lengths of time in order to find out how long the sample may be held before the determination is made. (Table I.) The sample was centrifuged for varying lengths of time to see if there was a significant change with moderate variations in centrifugation. (Table II.) Determinations were made comparing results obtained with a sealed electrode and open type of electrode. (Table III.) Multiple determinations were made on twenty-five samples using the open electrode. (Table IV.) The maximum error in the split samples was pH 0.07. The average variation was plus or minus pH 0.03. These figures show that for the accuracy desired the blood may remain under oil for three hours and may be centrifuged for ten minutes without effecting the determination significantly. Values obtained with the use of sealed and open electrodes are so similar that the trouble of using the sealed electrode is not worth while. Since the determina-

TABLE I. VARIATIONS OF pH IN SAMPLES REMAINING UNDER OIL VARYING LENGTHS OF TIME

MINUTES				
15	60	120	240	360
7.5	7.48	7.5	7.58	7.6
7.36	7.42	7.42	7.46	7.52
7.42	7.45	7.44	7.48	7.48
7.48	7.44	7.5	7.52	7.57
7.22	7.25	7.3	7.36	7.37
7.51	7.56	7.55	7.6	7.58
7.49	7.43	7.5	7.51	7.57
7.32	7.32	7.38	7.4	7.42
7.58	7.5	7.53	7.56	7.7
7.53	7.51	7.55	7.56	7.6

TABLE II. VARIATIONS OF pH IN SAMPLES CENTRIFUGED VARYING LENGTHS OF TIME

MINUTES CENTRIFUGED	SAMPLE									
	1	2	3	4	5	6	7	8	9	10
5	0	7.36	7.46	7.4	7.22	7.42	7.5	7.44	7.5	7.1
10	7.35	7.41	7.5	7.4	7.25	7.4	7.48	7.44	7.52	7.08
20	7.45	7.48	7.52	7.44	7.3	7.44	7.52	7.51	7.56	7.16

TABLE III. VARIATIONS OF pH WITH SEALED AND OPEN ELECTRODES

ELECTRODE	SAMPLE									
	1	2	3	4	5	6	7	8	9	10
Open electrode	7.32	7.45	7.41	7.48	7.48	7.42	7.48	7.22	7.08	7.45
Sealed electrode	7.35	7.45	7.35	7.48	7.48	7.46	7.5	7.2	7.13	7.4

TABLE IV. VARIATIONS OF pH IN SINGLE SAMPLES

7.52	7.5	7.46	7.5	7.45	7.5	7.48	7.52	7.64
7.5	7.52	7.42	7.46	7.4	7.48	7.48	7.52	7.61
7.45	7.5							
7.68	7.59	7.72	7.74	7.64	7.14	7.32	7.81	
7.68	7.58	7.68	7.72	7.61	7.1	7.3	7.79	
7.72	7.74	7.44	7.46	7.22	7.13	7.51	7.53	
7.68	7.72	7.42	7.42	7.2	7.08	7.5	7.51	

tion can be made several hours after the sample is drawn, the method is valuable because the sample can be obtained at the time the patient is admitted and can be run when the technician is available. No references could be found which indicated the variations which would be expected when the collection was made in the manner described.

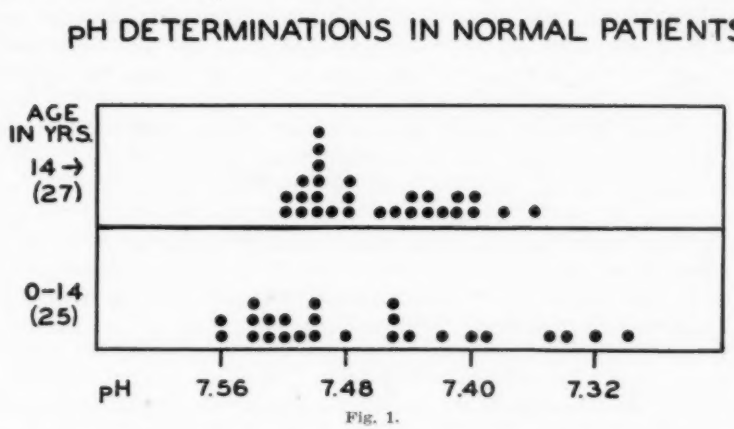

Fig. 1.

Normal values were obtained from people who had no disease process known to produce abnormalities in acid-base balance. (Fig. 1.) These values, which varied from 7.3 through 7.56, were slightly higher than the range of pH 7.33 through 7.51 which were accepted as normal by Earle and Cullen.[2] The slightly high values obtained were probably a result of the errors inherent in the method. A great majority of the determinations were done by a technician who had no previous training in handling biological materials.

COMMENTS

This method is not intended for exact determinations of the serum pH. Carbon dioxide is soluble in mineral oil. Therefore, the time the blood remains under oil and the speed and time of centrifugation should effect the diffusion of carbon dioxide. Glycolysis should alter the pH. However, empiric observations indicate that these factors do not alter the pH within the limits desired. Interfacial tension probably prevents the diffusion of carbon dioxide in spite of its relatively high solubility in mineral oil. Varying amounts of mineral oil did not alter the determinations.

This method has been checked by bedside determinations on whole blood and on heparinized blood. These determinations have checked closely with simultaneous ones done by the method described above. It has also been checked on patients with known alkalosis and acidosis. The determinations in these cases have fallen within limits which were expected from the clinical and laboratory data available.

This simple method for the determination of serum pH is applicable for use in a clinical laboratory. This method has proved to be practical since blood may be obtained at the time the studies are required and the blood can then be held until the technician can be called. It does not demand that the technician be present at all times, and does not require special preparation of equipment before the blood is obtained. A technician who has had average training can get consistent results. This method cannot be used for purposes such as in the calculation of the carbon-dioxide tension where determinations of accuracy greater than pH 0.05 is required, but is of great aid in differentiating alkalosis from acidosis and in indicating the degree of decompensation of the acid-base balance.

The sample can remain under oil for three hours and may be centrifuged for ten minutes without significantly altering the determination.

SUMMARY

A method for the determination of serum pH which is applicable for use in a clinical laboratory is described.

The effects of various factors on serum pH determinations are described.

Normal values obtained by this method are given.

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EFFECT OF TERMINAL DISINFECTION AND OTHER FACTORS ON THE STABILITY OF ASCORBIC ACID IN RELIQUEFIED MILK PRODUCTS USED IN INFANT FEEDING

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THE terminal disinfection of milk formulas for infant feeding has been suggested as a standard procedure for hospital formula rooms. It seems advisable that any adopted technique be based upon a time-temperature treatment that will effect the necessary microbial and toxin inactivation with a minimum loss of factors important in the nutrition of the infant. Ascorbic acid (vitamin C) is one of these factors that is readily destroyed by oxidation. Although the vitamin, when in aqueous solution, is stable to heat if oxidizing substances including dissolved oxygen are absent, heating accelerates the oxidation when oxidizing substances are present. The purpose of this investigation, therefore, was to study the effect of various temperature treatments and certain other influencing factors upon the stability of ascorbic acid in formulas for infant feeding made from fortified milk powders.

The literature pertaining to the stability of ascorbic acid in milk, to the effect of processing treatments, and to the oxidative catalysts is extensive. Most of the investigational work, however, has dealt primarily with the stability of the naturally occurring vitamin. The few available data concerning milk products fortified with synthetic ascorbic acid have been collected from studies of fluid market milk or evaporated milk. Although such information may not be directly applicable to the stability of the vitamin in a reliquefied powdered milk product, a brief review of the literature on this limited phase of the subject is presented.

Woessner, Weckel, and Schuette[1] showed that pasteurizing unfortified and fortified fluid milk at 145° to 150° F. for thirty minutes caused an approximate 20 per cent loss of total ascorbic acid. Their data show that the destruction of ascorbic acid appears to be more dependent on the time the milk is held at an elevated temperature than on the temperature itself. They conclude that vitamin C fortification of fluid milk is practical if contamination with copper is rigidly prevented and the milk is protected from light.

Calculations from data presented by Hartman[2] showed that freshly pasteurized mixed herd milk lost 16 per cent of its natural reduced ascorbic acid during the first forty-eight hours of storage at approximately 40° F. The rate of loss was 0.06 mg. per liter of milk per hour. Some of the same milk fortified with 25 mg. of synthetic ascorbic acid per liter lost only 10 per cent of its reduced ascorbic acid during the first forty-eight hours of storage. The rate of loss, however, was 0.09 mg. per liter per hour. Some of the same milk intentionally contaminated with 6.4 ppm. copper, but containing no synthetic

From the M and R Dietetic Laboratories, Inc.

ascorbic acid, lost 87 per cent of its reduced ascorbic acid during the first two hours of storage. The rate of loss was 8.5 mg. per liter per hour. The same copper-contaminated milk, to which 25 mg. of synthetic ascorbic per liter was added, lost 62 per cent of its reduced ascorbic acid during the first two hours of storage. The rate of loss, however, was 13.9 mg. per liter per hour.

Holmes and Jones[3] reported that an 11 per cent loss of reduced ascorbic acid per day during the first three days of refrigerator storage occurred in raw cow's milk that had been fortified with ascorbic acid at the rate of 75 mg. per liter. These investigators also observed that milk fortified with 150 mg. of ascorbic acid per liter lost an average of 6 per cent per day under the same conditions. It will be noted that the loss of ascorbic acid in milligrams per hour was a little greater in the case of the higher fortification.

Josephson and Doan[4] concluded from their studies that it is commercially feasible to fortify evaporated milk with ascorbic acid provided the cans are vacuum sealed.

Spray-dried fat-containing milk products are customarily packaged in hermetically sealed containers in inert gas after first being subjected to high vacuum. Such procedure, while originally instituted as a means of inhibiting lipid oxidation, can be anticipated as serving to increase the stability of the ascorbic acid present in dried milk products. Results obtained in our laboratory showed that milk powders packaged in this manner lost only 2.7 per cent of their total ascorbic acid during one year of storage. The product, when packaged, contained 296 mg. of ascorbic acid per pound and one year later contained 288 mg. per pound.

EXPERIMENTAL PROCEDURES

The dried milk product* used in this study was one of the products designed especially for infant feeding. The composition of this product is 13.75 per cent protein, 26.85 per cent fat, 52.90 per cent lactose, 4.50 per cent ash, and 2.0 per cent moisture. All samples used in this study were fortified with synthetic crystalline ascorbic acid, the ascorbic acid being added to the liquid product previous to drying. The batches of powder used were made in regular commercial operation by the spray drying process. The results obtained in this study, consequently, should be fairly representative of the product of commerce. A standard ratio for reliquefying the powder was used throughout the investigation, the ratio being ¼ lb. powder made up to one quart of liquid with warm water.

All formula samples, after having been subjected to the various treatments described herein, were placed in an ordinary household electric refrigerator for storage until analyzed for ascorbic acid content. Since it is common practice, both in the home and in the hospital, to prepare a twenty-four-hour formula feeding requirement at one time and to store the bottles until used, the investigational data herein reported were collected twenty-four hours after reliquefaction of the milk powder, unless otherwise specified. It was felt that such a procedure would allow a more reliable estimation to be made of the minimum amount of ascorbic acid being consumed by the infant in a twenty-four-hour period.

*Similac.

The analytical procedure used for determining reduced ascorbic acid was a modification of the Mindlin and Butler[5] procedure as described by Woessner, Elvehjem, and Schuette.[6, 7] The Willberg[8] solution as modified by Woessner, Elvehjem, and Schuette[6, 7] was used for producing a clarified serum and to prevent oxidation of the ascorbic acid except that produced by the indophenol reagent. The procedure used for determining the dehydro form of the vitamin was essentially the same as that described by these same investigators.[6, 7]

It will be seen from data presented later in this paper on formula samples subjected to heat that the ascorbic acid content after twenty-four hours appeared to be comparatively quite high. It was thought that perhaps spurious heat-generated reducing substances were reacting with the indophenol reagent to give these high values. A determination for interfering reductones, as these compounds are collectively termed by some workers, according to the method of Robinson and Stotz as given by Rubin, Jahns, and Bauernfeind[9] gave negative results. Josephson and Doan[4] stated that the acid precipitation and filtration procedure which they used removed all interfering nonascorbic acid reducing substances. Since their procedure was quite similar to that used in this investigation, it may be taken as evidence substantiating a claim of the absence of interfering reductones.

Heat Treatments.—After reliquefaction, the liquid formulas were transferred to 8-ounce nursing bottles (unless otherwise specified), stoppered, and treated as indicated in the accompanying tables of experimental results. Those treatments designated "A. S. Co." were heat treated in accordance with the procedure for terminal disinfection recommended by the American Sterilizer Co.; the procedure is essentially that used at Children's Hospital* in Columbus, Ohio. The specific procedure used in these studies consisted in placing the formula bottles in the sterilizer, raising the temperature inside the sterilizer with flowing steam to 180° F. in two minutes and to at least 190° F. within five minutes after heating started, and thereafter allowing the sterilizer temperature to increase slowly toward 210 to 212° F. during the remainder of the heating period. The indicated heating times given with the "A. S. Co." data in Tables II and III designate the period during which the temperature inside the sterilizer was at 180° F., or above. The actual temperature of the formula following such treatment was 180° F. in the case of a seven-minute exposure and 205 to 210° F. for fifteen minutes' exposure.

The heated samples were cooled to about 70° F. in cold water immediately after the indicated heat treatment unless otherwise specified. In order to determine what effect slower cooling has upon ascorbic acid losses, samples were allowed to stand in the laboratory, under ordinary summer temperature conditions, protected from light for three hours after removal from the sterilizer. Since ascorbic acid is known to be photolabile, the effect of three-hour exposures to the diffuse light of the laboratory was determined and compared with the previously described light-protected samples.

*We wish to thank Dr. Warren Wheeler of Children's Hospital for his interest and kindly cooperation in this study.

Copper, Iron, Chlorine.—The effect of copper on ascorbic acid in solution is well established. Somewhat less information is available concerning the effect of iron. Chlorine, being an oxidizing agent, conceivably might affect the stability of ascorbic acid in solution. In order to study the effect of these substances, formulas were made up with waters intentionally contaminated, respectively, with copper (as copper chloride), iron (as ferrous sulfate), and chlorine (as calcium hypochlorite) and the results compared with those obtained on untreated control samples.

Warming the Refrigerator-Stored Formulas.—Since it is general practice to warm formulas held in the refrigerator previous to feeding to body temperature, this procedure was followed in some trials and the ascorbic acid content was compared with that of samples not so treated.

Stability of Ascorbic Acid in Open Cans of the Powder.—A number of cans of the powder were analyzed for ascorbic acid immediately after opening and periodically thereafter for eight to ten days. The lids were loosely placed on the cans during this period so as to protect the contents from exposure to light.

EXPERIMENTAL RESULTS

The average reduced ascorbic content of the freshly opened cans of the dried milk product was 300 mg. per pound and the average total ascorbic acid was 323 mg. per pound. The average losses four days after opening the cans, the top layer being removed daily for analysis (the average length of time a can containing one pound of the dried product remains open before its contents are completely used in feeding an infant is about four days) were 2.8 per cent of the reduced ascorbic acid and 3.2 per cent of the total ascorbic acid. The average losses eight days after opening the cans were 6.3 per cent and 6.7 per cent of the reduced and total ascorbic acid, respectively.

Table I shows the amount of ascorbic acid in one quart of the reliquefied product (¼ lb. of powder made to one quart of liquid) when freshly made up and after being held twenty-four hours in an electric refrigerator.

TABLE I. ASCORBIC ACID CONTENT OF FRESHLY RELIQUEFIED PRODUCT AND AFTER TWENTY-FOUR HOURS REFRIGERATOR STORAGE

	MG. ASCORBIC ACID PER QUART		PER CENT LOSS	
	REDUCED	TOTAL	REDUCED	TOTAL
Freshly made	71.4	77.2	---	---
24-hour storage	62.8	68.6	12.0	11.1

The effects of various heat treatments, cooling procedures, and exposure to diffused daylight on the ascorbic acid content of reliquefied product are shown by the data in Table II. The values given are the concentrations of ascorbic acid in the formulas immediately after reliquefaction and twenty-four hours after reliquefaction. All samples were held in the electric refrigerator after receiving the treatments indicated in the table until ready for analysis.

A formula contained in stoppered nursing bottles heated at 230° F. (about 7 lb. pressure) for fifteen minutes, cooled in ice water quickly, and analyzed immediately, lost 8.0 per cent and 13.6 per cent of its reduced and total

ascorbic acid, respectively. Nursing bottles containing a formula were heated by immersion in a boiling water bath for fifteen minutes, quickly cooled in ice water, and the formula was analyzed immediately thereafter. The formula

TABLE II. ASCORBIC ACID CONTENT OF VARIOUSLY TREATED PRODUCT FORMULAS IMMEDIATELY AFTER AND TWENTY-FOUR HOURS AFTER RELIQUEFACTION

FORMULA TREATMENT	MG. ASCORBIC ACID PER QUART				% LOSS IN 24 HR.	
	0 HR.		24 HR.			
	REDUCED	TOTAL	REDUCED	TOTAL	REDUCED	TOTAL
1—A. S. Co., 7 min.; cooled quickly.	71.8	76.9	54.8	62.0	23.7	19.4
2—A. S. Co., 7 min.; room temp. 3 hr., protected from light.	71.8	76.9	54.5	58.9	24.1	23.4
3—A. S. Co., 15 min.; cooled quickly.	71.8	76.9	55.2	62.0	23.1	19.4
4—A. S. Co., 15 min.; room temp. 3 hr., protected from light.	71.8	76.9	55.2	59.3	23.1	22.9
5—Heated in water bath, temp. raised from 180° to 200° F. in 10 min.; cooled quickly.	70.6	76.0	56.4	59.7	20.1	21.4
6—Heated as No. 5; room temp. 3 hr., protected from light.	70.3	75.1	53.4	57.2	24.0	23.8
7—Heated as No. 5; room temp. 3 hr., exposed to diffused light.	70.3	75.1	51.7	54.5	26.5	27.4
8—Heated as No. 5; room temp. 18 hr., protected from light.	71.4	78.6	51.7	54.3	27.6	30.9
9—Heated at 230° F. (7 lb. press.) for 5 min.; cooled quickly.	71.4	79.6	64.1	67.7	10.2	14.9
10—Heated as No. 9; room temp. 3 hr., protected from light.	71.4	79.6	64.1	66.2	10.2	16.8
11—Heated at 230° F. (7 lb. press.) 15 min.; cooled quickly.	72.4	77.8	60.2	64.1	16.9	17.6
12—Heated in boiling water bath 15 min.; cooled quickly.	72.4	78.1	56.1	62.0	22.5	20.6

TABLE III. EFFECT OF ADDING COPPER, IRON, AND CHLORINE ON THE STABILITY OF ASCORBIC ACID IN RELIQUEFIED DRY MILK PRODUCT

FORMULA TREATMENT	MG. ASCORBIC ACID PER QUART				% LOSS IN 24 HR.	
	0 HR.		24 HR.			
	REDUCED	TOTAL	REDUCED	TOTAL	REDUCED	TOTAL
1—1 ppm. Cu; not heated.	76.5	84.8	29.0	37.2	62.1	56.1
2—1 ppm. Cu; heated at 190° F. for 5 min.	76.5	84.8	23.8	24.8	69.3	70.8
3—0.5 ppm. Cu; not heated.	77.6	84.8	45.5	47.6	51.4	43.9
4—0.1 ppm. Cu; A. S. Co., 15 min.; room temp. 3 hr. protected from light.	*	77.6	*	61.0	*	21.4
5—0.2 ppm. Cu; otherwise as No. 4	*	77.6	*	57.9	*	25.4
6—0.2 ppm. Cu; not heated.	*	77.6	*	53.8	*	30.7
7—1 ppm. Fe^{++}; A. S. Co., 15 min.; room temp. 3 hr. protected from light.	*	78.6	*	60.0	*	23.7
8—2 ppm. Fe^{++}; otherwise as No. 7.	*	78.6	*	58.9	*	25.1
9—1 ppm. Fe^{++}; not heated.	*	84.8	*	69.3	*	18.3
10—2.5 ppm. Cl added; not heated.	70.8	75.5	66.2	67.7	6.5	10.3
11—5 ppm. Cl added; not heated.	72.4	75.5	63.1	67.2	12.8	11.0
12—10 ppm. Cl added; not heated.	69.3	77.6	57.9	65.2	16.5	16.0
13—10 ppm. Cl added; heated in boiling water bath for 15 min.	69.3	77.6	54.8	55.8	20.9	28.1
14—25 ppm. Cl added; not heated.	67.2	74.5	45.0	52.7	33.0	29.3
15—25 ppm. Cl added; heated at 230° F. (7 lbs. press.) for 15 min.; cooled quickly.	65.2	71.4	43.4	48.6	33.4	31.9

*Reduced ascorbic acid not determined.

lost 14.7 per cent and 17.3 per cent of its reduced and total ascorbic acid, respectively. The same formula, contained in an open vessel, was heated directly over an open flame, cooled quickly in an ice water bath, and analyzed immediately. The formula lost 6.7 per cent and 9.9 per cent of its reduced and total ascorbic acid, respectively.

The effects of added copper, iron, and chlorine on the ascorbic acid content of the reliquefied product are shown by the data in Table III.

Warming stored samples of the formula to body temperature just prior to analysis caused no decrease in the concentration of ascorbic acid. When such warmed samples were allowed to stand in a boiling water bath for five minutes, or longer, the ascorbic acid concentration was decreased by as much as 15 per cent.

DISCUSSION

The loss of ascorbic acid in an opened one-pound can of the dried milk product is negligible at the end of four days, which is the usual length of time a can of the product remains open in the home. The average loss in the reliquefied product (unheated after makeup) during twenty-four hours of refrigerator storage is about the same as that reported by Holmes and Jones[3] for fluid milk fortified with 75 mg. of ascorbic acid per liter.

The data in Table II show that fast heating at high temperatures for the purpose of terminal disinfection of the infant feeding formula is less destructive of ascorbic acid than is slower heating at lower temperatures. There appears to be considerable loss of ascorbic acid during the heating procedure but during storage less loss is experienced than in unheated samples.

Slightly greater loss of ascorbic acid occurred in samples of the reliquefied product allowed to cool slowly to room temperature before being placed in the refrigerator than occurred in quickly cooled samples. Likewise, exposure of the formulas to diffused daylight accelerated destruction of the vitamin. This factor is primarily a function of light intensity; consequently, the degree of ascorbic acid destruction as influenced by this factor would be expected to vary from day to day.

The data in Table III show that the addition of 0.1 ppm. of soluble copper to the water used in making up the formulas had essentially no effect on the destruction of ascorbic acid during the heating of the formulas, but that 0.2 ppm. did accelerate the destruction slightly. Addition of larger quantities of copper to water used in the formulas caused drastic losses. It is interesting to note that heated formulas containing 0.2 ppm. copper suffered less ascorbic acid loss than did unheated formulas containing a like amount of copper, whereas heated samples containing 1 ppm. copper lost more of the vitamin than did the unheated samples containing 1 ppm. copper. The explanation for this fact is not readily apparent from these few data, but it may be that at low levels the effect of copper as an oxidative catalyst can be minimized by heat treatment, the copper possibly being bound by protein to form an inactive complex. At higher copper levels the destructive action of copper and heat appears to be additive.

The presence of 1 or 2 ppm. of added iron slightly increased the losses of ascorbic acid in heated formulas but concentrations of iron of these magnitudes seldom, if ever, would be found in water used in making up the formulas.

Chlorine in concentrations as high as 5 ppm. had no discernible effect on the loss of ascorbic acid during storage of the samples. In greater concentration a definite effect was noted. However, the residual chlorine content of the drinking waters of Columbus, Ohio, is usually less than 0.1 ppm. and in no instance is a 5 ppm. content to be expected in water used for making up a feeding formula.

SUMMARY

The following general observations are drawn from the data collected during the course of this investigation:

1. Loss of ascorbic acid in the dry powder contained in the opened can appears to be negligible during the first four days.

2. Reliquefied formulas made from dried milk products of the type used in these studies, containing approximately 75 mg. of total ascorbic acid per quart, and prepared in the conventional manner without heating, lose approximately 11 per cent (about 8 mg.) of their total ascorbic acid content during twenty-four hours of storage under ordinary home refrigeration.

3. Terminally disinfected formulas (originally containing about 75 mg. total ascorbic acid per quart) which have been rapidly cooled before being put under refrigeration lose approximately 15 to 20 per cent (about 11 to 15 mg.) of their total ascorbic acid content during the combined heating and storage period of twenty-four hours.

4. Terminally disinfected formulas allowed to cool slowly lose slightly more of their total ascorbic acid content than if cooled rapidly.

5. Terminal disinfection of the formula by the fast heating high temperature procedure is to be preferred with respect to the stability of ascorbic acid.

6. Warming the refrigerated formula quickly to body temperature just prior to feeding does not increase the loss of ascorbic acid.

7. Exposure of the reliquefied product to light for extended periods of time accelerates the loss of ascorbic acid and is to be avoided.

8. Iron and chlorine in the amounts normally present in treated city waters have no significant effect on the stability of the ascorbic acid in the formulas.

9. Contamination of the water used in making up the formulas with copper generally accelerates the loss of ascorbic acid. Therefore, boiling the water subsequently to be used in making up the formulas in copper vessels is not desirable.

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Case Reports

EMBRYOMA OF CONTRALATERAL KIDNEY TEN YEARS FOLLOWING NEPHRECTOMY FOR WILMS' TUMOR

JOSEPH A. RITTER, M.D., AND EARL S. SCOTT, M.D.
PHILADELPHIA, PA.

EMBRYOMA affecting both kidneys occurs rarely. Such involvement is manifested early or may be an incidental finding at necropsy (Walker,[1] Sheldon and Canaday,[2] Fusaro,[3] Campbell[4]). The origin of bilateral tumors is a matter of conjecture. Dean and Pack,[5] in referring to bilateral neoplasms in paired organs of children, question the use of the term *metastatic* because of the manner in which such tumors usually spread.

The case herein reported is of special interest and warrants presentation because the contralateral kidney was involved by embryoma ten years after nephrectomy for a similar tumor. Of additional interest is the fact that the patient died not as a direct result of the tumor but because of renal failure associated with diffuse renal fibrosis. Roentgen therapy apparently successfully destroyed the tumor tissue, but in so doing it is possible that it produced irreversible damage in the remnant normal kidney parenchyma.

W. A., a 10-year-old white boy, was admitted to the Pediatric Ward of the Graduate Hospital on Jan. 6, 1947, because of pain in the left flank of three days' duration and a vague history of an episode of hematuria which his mother attributed to trauma.

The past medical history revealed normal development until 5½ months of age when the patient became constipated and a mass was discovered in the right abdomen. A diagnosis of embryoma was made and confirmed by pathologic examination following right nephrectomy. (Fig. 1.)

The child progressed normally for approximately ten years, when pain occurred in his left flank and his mother felt a large tumor. He was admitted to the hospital three days later. On admission a large, firm, nontender mass was felt which filled the left abdomen from the costal margin to the crest of the ilium, and extended to the midabdominal area. The scar of the previous nephrectomy was evident in the right flank. Small, generalized adenopathy and an active ethmoiditis were discerned. The lungs were negative on physical examination. A systolic murmur was heard at the base of the heart. No cardiac hypertrophy was noted and the rhythm was normal. Blood pressure during this admission ranged between 130/70 and 134/90 mm. mercury. Funduscopic examination was negative.

Urinalysis was negative on three occasions. The red blood cell count numbered 3,910,000 cells per cubic millimeter and the leucocytes 11,900 cells per cubic millimeter. The differential count was normal. Hemoglobin content of the blood was 11 Gm. per 100 c.c. (66 per cent). The hematocrit reading was 32 volumes per cent. Blood urea nitrogen was 18 mg., chlorides 584 mg., cholesterol 280 mg., and total protein 6.8 Gm. per 100 c.c. of blood, respectively. The carbon-dioxide combining power was 49 volumes per cent and the alkaline phosphatase 3.8 Bodansky units.

From the Department of Pediatrics, Graduate Hospital of the University of Pennsylvania.

An x-ray film of the abdomen showed an increased density in the left upper quadrant which could not be outlined definitely. Intravenous urography demonstrated good renal function but marked deformity of the upper calices and infundibula. The entire excretory system of the kidney was pushed downward and forward by a rather large mass. (Fig. 2.)

The patient's stay in the hospital was uneventful. His temperature, which was 101° F. orally on admission, continued in septic form until it fell by lysis to a normal level on Jan. 15, 1947. He was discharged Jan. 22, to be treated as an outpatient by the X-ray Department.

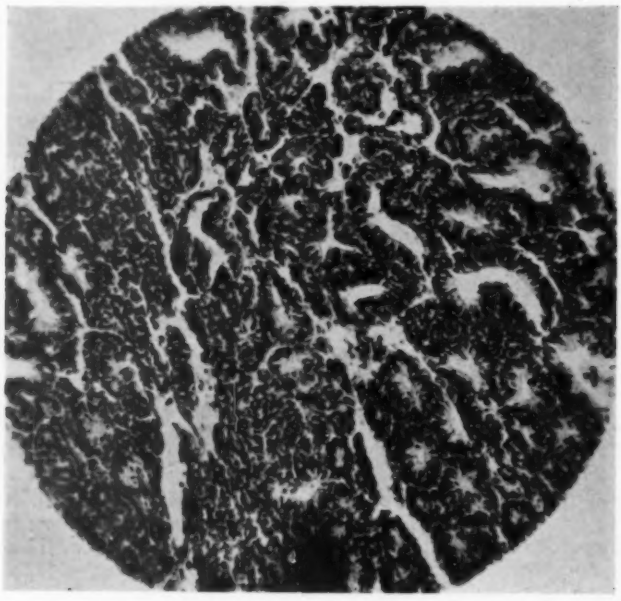

Fig. 1.—Microphotograph (×200) showing glandular-like formation of the tumor mass involving the right kidney (nephrectomy performed June 21, 1937).

During the course of x-ray therapy he developed nausea, vomiting, headache, and increasing pallor. A blood count revealed 2,770,000 red blood cells per cubic millimeter with a hemoglobin content of 7.5 Gm. per 100 c.c. of blood. A total of 6,400 roentgen units had been administered to the tumor area when he was readmitted to the hospital on Sept. 29, 1947.

On this admission examination revealed generalized edema, extreme pallor, and slight nuchal rigidity. His weight was 72½ pounds, an increase of 11 pounds since his discharge on Jan. 22, 1947. A loud, systolic murmur was heard over the base of the heart and the second aortic sound was accentuated. Cardiac hypertrophy was evident on palpation and percussion. The blood pressure was 230/170 mm. mercury. No tumor mass could be felt in the abdomen. Funduscopic examination revealed pallor of both discs, exudate in the right retina and hemorrhage in the left.

Laboratory examination revealed a fixed specific gravity of the urine ranging from 1.010 to 1.013. The urines were acid in reaction and devoid of albumin. Blood urea nitrogen was 60 mg. per 100 c.c. of blood on admission and thereafter ranged to 125 mg. Blood creatinine, which was initially 3.4 mg. per 100

c.c. of blood, varied between 11 and 11.3 mg. The blood cholesterol was 268 mg. and cholesterol esters 186 mg. per cent. Blood calcium was 10 mg. per cent, phosphorus 3.3 mg. per cent, and alkaline phosphatase 2.2 Bodansky units. Serum bilirubin measured 0.3 mg., blood sugar 109 mg., plasma chlorides 556 mg. per cent, while total blood protein measured 5.6 Gm. per 100 c.c. of blood with an albumin value of 2.52 and a globulin value of 3.08 Gm. per cent, respectively. X-ray examination of the skeleton on Sept. 30, 1947, was negative for any evidence of metastases. The chest x-ray films showed a moderate degree of left ventricular enlargement with increased prominence of the aortic knob. The lungs were essentially negative. Intravenous urography failed to reveal any excretion of dye during an observation period of one hour and fifteen minutes, indicating a markedly decreased excretory function of the left kidney. An

Fig. 2.—Intravenous urogram revealing downward and forward displacement of left kidney (Jan. 7, 1947).

electrocardiogram on Oct. 8, 1947, revealed the following: The auricular and ventricular rate were both 108. The P-R interval was 0.12 second and a sinus tachycardia was evident. The P waves and QRS complexes were normal while the RS-T segments were elevated in CR_2. The T waves were of low amplitude in CR_2 and CR_3. These findings were interpreted to indicate some myocardial abnormality and probable left ventricular hypertrophy. The configuration of the T waves in the precordial leads suggested a high level of potassium in the blood.

During this admission the patient was oliguric and vomited at least once daily. His blood pressure ranged from 210/170 to 220/180 mm. Hg. He desired to be ambulatory, and in view of the obvious outcome, this was permitted until intense vertigo on Oct. 8, 1947, precluded him from leaving bed. The next day

he became unconscious. Examination revealed nuchal rigidity, opisthotonus, trismus, and contracted pupils. Tachycardia was present and the blood pressure was 260/170 mm. Hg. Breathing was stertorous and râles could be heard throughout the lungs. The spinal fluid was bloody and under considerable pressure. Therapy, which included two transfusions, hot packs, phenobarbital sodium and magnesium sulfate intramuscularly, and glucose and saline intravenously, was of no avail and he expired four hours after the onset of coma, Oct. 9, 1947.

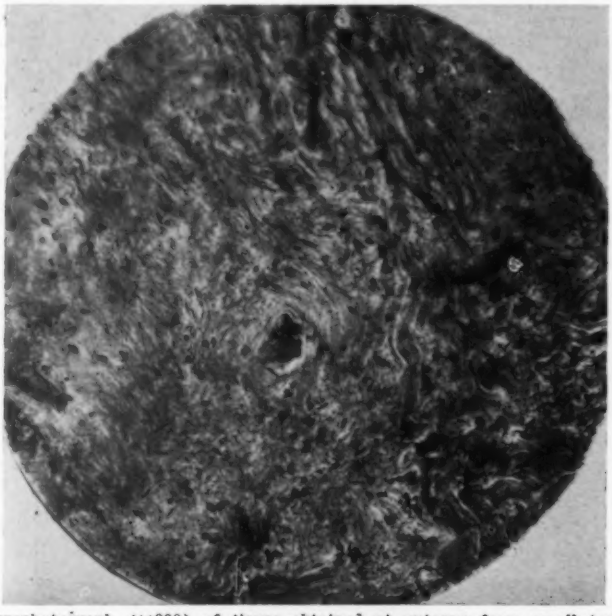

Fig. 3.—Microphotograph (×200) of tissue obtained at autopsy from small tumor mass on mid-anterior surface of left kidney. (Note marked fibrosis.)

Autopsy was restricted to the left kidney area and was done by Dr. L. L. Adamkiewicz. The abdominal cavity contained about 200 c.c. of clear, straw-colored fluid. Diffuse congestion was noted in the omentum. The left kidney weighed 240 Gm., was normal in outline, and was not adherent to surrounding tissues. The left adrenal was markedly compressed and weighed 3 Gm. The kidney measured 14 cm. in length, 6.5 cm. in width, and 3.5 cm. in thickness. A yellowish tumor, slightly raised and buttonlike, and measuring 2.5 cm. by 2.5 cm., was found 6 cm. from the lower pole on the mid-anterior surface. (Fig. 3.) On section a large tumor mass measuring 6 cm. by 6.5 cm. by 3.5 cm. with a necrotic center was seen in the substance of the upper pole of the kidney. The tumor was pale yellow in color and uniform in texture beyond the necrotic center. It was infiltrative and a wide, fibrous band separated it from the kidney tissue. Microscopic examination showed an alveolar arrangement of slightly oval cells with a small amount of cytoplasm. These cells were of uniform size and mainly of low cuboidal shape. The nuclei stained moderately deep and showed occasional small nucleoli. Fibrous tissue, composing a supporting stroma, surrounded the epithelial cells, which were single or in acinar formation. There were also wide bands of fibrous tissue encapsulating the growth. The latter

was invaded by collections of round cells and a few plasma cells. There were many areas of calcification in the fibrous tissue capsule. The cellular elements often seen in this type of tumor were no longer evident, possibly as a result of the intensive x-ray therapy. The microscopic picture was one of marked fibrosis. The necrotic area in the central portion of the growth had the characteristics of necrosis due to deficient blood supply. The smaller tumor had the same morphology as the larger one except that no necrosis was present. The outstanding picture in the kidney was that of an extensive arteriolar nephrosclerosis with extensive hyalinization.

DISCUSSION

Prognosis following nephrectomy because of embryoma depends on recurrence and metastases. In a series of sixty cases reported by Ladd and White,[6] recurrence occurred in thirty-two instances and of these thirty-one occurred within nine months after operation. The longest interval for recognition of recurrence was twenty months. The postoperative mortality rate within a three-year period is variously reported to range from 42 to over 70 per cent (Ladd and White,[6] Priestley,[7] Nesbit and Adams,[8] Higgins and Shively[9]) with one survival up to 41 years. (Higgins and Shively.[9]) Embryoma occurring in a contralateral kidney approximately ten years after nephrectomy for a similar tumor is a rare occurrence.

Tumors of this variety are notoriously radiosensitive and roentgen therapy is at times employed preoperatively and postoperatively. It remains the only form of treatment in cases not amenable to surgery. In our case the x-ray therapy may have contributed to the development of sclerosis and fibrosis and thereby accelerated the progression of the disease process in the remnant kidney. The establishment of an artificial kidney mechanism was considered but was not deemed suitable in a situation of this nature.

SUMMARY

1. A case is reported in which a contralateral kidney was apparently involved by embryoma approximately ten years after nephrectomy for a similar tumor.

2. Roentgen therapy produced a remarkable reduction in the size of the tumor but may have contributed to the fibrosis and other changes which finally resulted in the death of the patient from renal failure.

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BILATERAL OPTIC NEURITIS FOLLOWING CHICKEN POX

Report of Case with Apparently Complete Recovery

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NEUROLOGICAL symptoms after chicken pox are relatively rare. A great variety of symptoms have been reported, including unconsciousness, delirium, tremors, ataxia, cerebellar syndromes, spinal paraplegias, etc. Cranial nerve palsies have occurred, usually combined with other symptoms. Involvement of the optic nerve has been reported by Ford. Bilateral involvement of the optic nerves without other symptoms may not have been seen. This case is presented because of its rarity and interest.

CASE REPORT

About March 28, 1948, a 5-year-old white male child developed chicken pox. He had a generalized eruption but was not particularly ill. He was restricted to bed for the first week and his convalescence seemed uneventful.

Two weeks after the onset, he was heard to complain that it was dark outside and the next day he complained of darkness in the house. Within the next few days he became unable to find food set in front of him and was unable to find the fork and spoon to eat.

The early development and family history are irrelevant.

Physical examination showed a well-developed, well-nourished child of 5 years, weight 44½ pounds, height 44½ inches, temperature 99.2° F. (R). Eyes showed bilaterally engorged retinal veins and elevated discs. Vision, especially central vision, was markedly impaired. He was able to distinguish dark and light, but fingers held before the eyes could not be counted.

The remainder of physical examination was essentially negative. There were no stiff neck, reflex changes, or other nerves involved.

The patient was seen by a local ophthalmologist who confirmed the eye findings and recommended neurological consultation because of the possibility of an intracranial neoplasm. We believed it to be a postvaricella encephalitic picture limited to the optic nerves. Because of the rarity of this condition, the child was sent to the Pediatric Department of the University of Utah Medical School, where he was examined by Dr. C. Harrison Snyder of the Department of Pediatrics and Dr. Alan Crandall of Ophthalmology Department. Their findings confirmed the visual changes and an elevated disc of 3½ D. bilaterally with appearance of papillitis.

Laboratory studies on April 18, 1948, revealed hemoglobin of 16.2 Gm. per 100 c.c. and red blood cells 6,010,000 per cubic millimeter. The hematocrit was 44 per cent packed cells, with an Wintrobe erythrocyte sedimentation rate of 5 mm. per hour. White blood count was 12,700, polymorphonuclears were 47 per cent, eosinophiles 2 per cent, basophiles 1 per cent, lymphocytes 47 per cent, and monocytes 3 per cent. Examination of the spinal fluid showed a pressure of 165 mm. of water, Queckenstedt sign was normal bilaterally, there were no cells, negative pandy, and normal protein. Electroencephalogram was within normal limits.

The vision remained very poor for two weeks and then began to improve very slowly. Within a week after the vision had begun to return, a test of

From the Hatch Clinic, Idaho Falls.

20/50 was obtained in each eye. Six weeks after the beginning of the blindness 20/30 vision was found bilaterally and the nerve heads were practically normal in appearance.

Thereafter no further improvement in vision occurred. The patient felt well subjectively all the time. The vision previous to the illness was not known.

SUMMARY

The case is presented of a 5-year-old child with bilateral optic neuritis developing marked impairment of vision two weeks after chicken pox. There was almost complete recovery within two months.

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CONGENITAL ABSENCE OF THE PATELLAE

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INTERMITTENLY, during the past fifty years, cases of congenital absence or dysplasia of the patellae associated with dystrophy of the nails and impaired function of the elbows have been reported in the medical literature. This triad is both hereditary and congenital. Almost all of the cases reported have a marked familial occurrence which indicates the hereditary etiology. It is apparently caused by a developmental defect of the mesodermal and ectodermal layers of the embryo.

Aschner[1] in 1934 offered an explanation as to why these defects occur separately or together in an individual. It is assumed there are separate pathologic factors responsible for each part of the triad since each may occur alone without the other. There is a close linkage in the same chromasome between the two genes which result in congenital patellar defects and dystrophy of the nails. Because of this close linkage, these two defects are almost always inherited together when present in a family. There is also a third pathologic factor which causes luxation of the head of the radius. This factor is in close proximity to the other two but not as close as the other two are to each other. For this reason luxation of the head of the radius does not occur as frequently as dystrophy of the nails and patellar defects. One can understand, therefore, why these three congenital defects can occur together or separately in the same individual or family.

In reviewing the literature, Senturia[4] and Mino and his collaborators[2] indicate that congenital absence of the patella has been reported almost invariably in association with one or both of the defects described above. Its occurrence alone is rare. The case here reported is unique because there is congenital absence of both patellae with no evidence of abnormality of the elbows or dystrophy of the nails. Three other siblings were examined but none of the defects of this triad was present. From the history obtained from the child's mother, the maternal family has been free of evidence of the triad. The only suspicion of its occurrence elsewhere in the child's family is found in a statement by the mother which indicated that the father of the child had "weak knees." Due to the separation of the parents, the present whereabouts of the father could not be ascertained.

CASE REPORT

S. C., a Negro girl, aged 9 years, was brought to the clinic by a welfare worker for a routine physical examination in September, 1948. At this time it was noted that the patient had no palpable or visible patellae.

From the Department of Roentgenology, Baltimore City Hospitals.

She is one of four living children, all of whom are well. One other child is dead. The father is living and well but has "weak knees." The mother is a patient in a tuberculosis sanitarium.

The birth history and habits are entirely noncontributory.

Fig. 1.—Genu valgum deformity.

Fig. 2.—Complete absence of both patellae, anterior view.

There is a history of measles, mumps, chickenpox, pertussis, and tonsillitis. It is known that the child has had "weak knees" since an early age because of her many falls.

On physical examination, she is 52 inches in height and weighs 52 pounds. In general she is rather undernourished. The only other positive findings are

as follows: There is some atrophy of the lower extremities. The knees appear rather flat anteriorly (Fig. 1) and the patellae are not palpable. There is a genu valgum deformity (Fig. 1). There is a faint basal systolic murmur audible over the heart. The lungs are clear. The spleen is barely palpable. The fingernails are normal. The child has full flexion of the elbows and they are normal in appearance.

X-ray examination of both knees verifies the absence of both patellae (Figs. 2 and 3). X-ray examination of both elbows shows no evidence of abnormality.

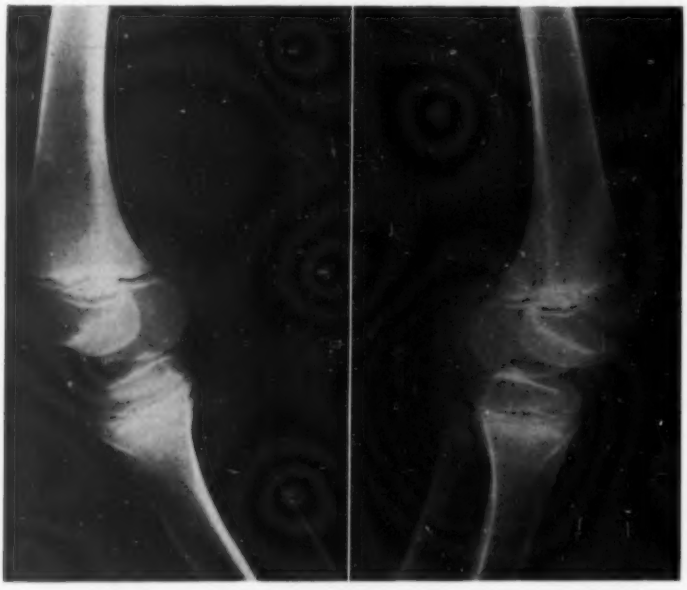

Fig. 3.—Complete absence of both patellae, lateral view.

SUMMARY

A unique case of congenital absence of the patellae in which there are no other associated abnormalities is presented. A brief review of the literature is presented with special reference to the explanation of the cause of this developmental defect.

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Clinical Conference

CONFERENCE AT THE NEW YORK HOSPITAL-CORNELL MEDICAL CENTER
JAN. 14, 1949

SAMUEL Z. LEVINE, PEDIATRICIAN-IN-CHIEF

DR. LEVINE.—According to our usual custom, the patient will not be in the room during the recounting of the history, physical and laboratory findings, and course in the hospital, but will be shown later. Dr. Mosher will present the first case.

Case 1. Hyperinsulinism

DR. THOMAS E. MOSHER (Resident in Pediatrics).—A. W., a white boy of 6½ years, is being presented on his third admission to the New York Hospital. He was first admitted at the age of 4½ years. The present illness apparently started shortly after birth. At 2 days of age he became comatose; there was no cyanosis or convulsions and he roused spontaneously after twelve hours. He thrived until 9 months of age when he had an uncomplicated pneumonia. At 10 months the patient had an episode of persistent vomiting and was hospitalized for three days; this symptom ceased following an infusion. At 14 months he had measles and again was hospitalized. From 2 to 3 years of age he had three episodes of persistent vomiting and drowsiness lasting two to three days. At 3 years of age these episodes became more severe and at times the boy could not be aroused. From 4 to 4½ years the attacks occurred every two weeks and by this time were characterized by two to three days of forgetfulness, clumsiness, stammering speech, awakening at night, vomiting, persistent drowsiness, and hypoglycemia.

The patient was admitted to the New York Hospital in January, 1947, at the age of 4½ years. Physical examination was unrevealing; roentgenograms of the skull, abdomen, and long bones were normal; electroencephalogram was essentially normal; a psychometric examination showed low average intelligence. His oral glucose tolerance test (2.2 Gm. per kilogram) was as follows:

Fasting	92 mg. %
½ hour	162 mg. %
1 hour	149 mg. %
2 hours	119 mg. %
3 hours	42 mg. %

His insulin sensitivity test (½ U per kilogram) was:

Fasting	89 mg. %
½ hour	42 mg. %
1 hour	31 mg. %
2 hours	26 mg. %

At the end of two hours he became drowsy and glucose was administered. His adrenalin tolerance test (0.01 ml. of 1:1000 per kg.) revealed:

Fasting	73 mg. %
½ hour	97 mg. %
1 hour	114 mg. %

His starvation test was as follows:

Fasting	87 mg. %
18 hours	62 mg. %
24 hours	36 mg. %
26 hours	29 mg. %

It was decided first to try medical management and he was sent home on a high protein diet and desiccated thyroid 15 mg. per day. The thyroid was discontinued by his private physician after a month. The patient was asymptomatic for five months; following a pharyngitis he again began to have the previously described episodes once a month and then with increasing frequency until at 5 years of age he had them twice a week. These were relieved by glucose infusions.

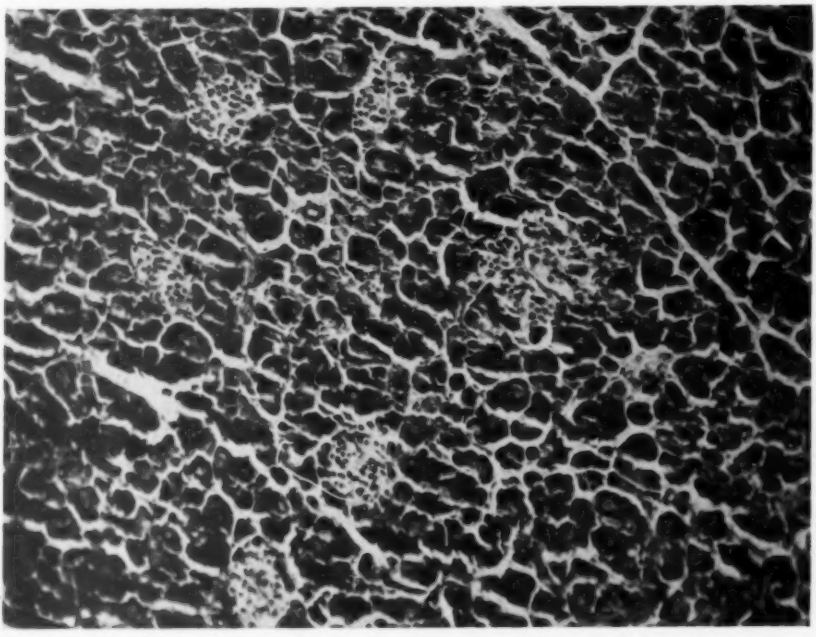

Fig. 1.—Case 1. Microscopic section of pancreas, January, 1948.

During his second admission to the New York Hospital in January, 1948, at 5½ years of age, all of the previous tests were repeated with essentially similar results. The I.Q. again was within the average range. Exploration was

decided upon but no pancreatic tumor was found. Approximately two-thirds of the pancreas was excised and microscopic sections revealed unrestricted proliferation of the islets of Langerhans, as many as 17 islets being seen in one low-power field (Fig. 1). The boy's postoperative course was uneventful. Repeat blood studies two weeks postoperatively showed no significant change from the initial values. He was sent home on a high protein diet. He was free from serious seizures for ten months following the operation, when he again lost consciousness, and following adrenalin and glucose he vomited and was drowsy the rest of the day. Thereafter these episodes recurred weekly and he was readmitted twelve days ago on Jan. 6, 1949, at 6½ years of age, one year following operation. Glucose, insulin, and adrenalin tolerance curves are essentially unchanged from those on his first admission. His electroencephalogram remains normal and his psychometric test, as before, shows a low average intelligence. During this two-week period of hospitalization he has had no seizures except those brought on by the insulin tolerance test.

DR. LEVINE.—There are two good reasons for presenting this patient. One is a consideration of differential diagnosis, which I hope Dr. Schloss will discuss in some detail. The other is the problem of therapy. Was exploratory laparotomy indicated and what should be our next therapeutic approach?

(Patient is brought in in a wheel chair)

DR. OSCAR M. SCHLOSS (Professor of Clinical Pediatrics).—Hello, Alan. How do you feel?

PATIENT.—Fine.

DR. SCHLOSS.—You can all see that this boy looks pretty well. He is a little undersized and slightly underweight. Inspection of his abdomen shows a transverse infraumbilical scar, the result of his operation done about a year ago. Are there any questions anyone would like to ask before he goes out?

STUDENT.—On what sort of diet is the patient now?

DR. MOSHER.—A high protein diet.

STUDENT.—Is his appetite normal or excessive?

DR. SCHLOSS.—Alan can answer that one. How is your appetite, Alan?

PATIENT.—It's O.K., I guess.

(Patient is taken out)

DR. SCHLOSS.—At the time of the first admission to this hospital it was already known that the patient suffered from recurring attacks of hypoglycemia accompanied by characteristic symptoms. He was admitted here with the thought that these episodes were perhaps due to a greatly increased or unopposed secretion of insulin and perhaps belonged to the group of cases amenable to surgery. Before this diagnosis could be seriously entertained it seemed necessary to exclude other causes of hypoglycemia by further observations and tests.

By most writers hypoglycemia of clinical importance is divided into the cases due to functional causes (actually of undisclosed origin) and those due to organic disease of organs participating in the intricate mechanism of sugar mobilization and metabolism.

At the outset it seemed possible to remove this boy's disease from the category of functional hypoglycemia. In the first place, his symptoms were more dramatic and severe than usually occur in the functional cases. In addition, his attacks occurred only after a long fast and not three to four hours after a carbohydrate meal. Also, his fasting blood sugar was frequently very low, which is rarely if ever observed in functional hypoglycemia, in which the lowest blood sugar usually appears after the insulin-stimulating effect of carbohydrate ingestion. It, therefore, seemed necessary to explore the organic diseases which could be responsible for this patient's hypoglycemic attacks.

There was no evidence from the history, laboratory tests, or examination that he was affected by the type of organic liver disease which may cause hypoglycemia. Furthermore, the normal size of the liver, the absence of ketone substances in the urine, and a positive response to the epinephrin test seemed sufficient to exclude the type of disease associated with immobility of liver glycogen seen in von Gierke's disease.

No disease or disturbance of function of the thyroid, adrenal cortex, or pituitary gland was disclosed and we felt that these causes of hypoglycemia could be excluded with reasonable assurance. There were no symptoms or physical signs, neurologic or otherwise, which seemed consistent with a thalamic lesion.

By this process of exclusion and by the positive evidence which has been presented in the history, laboratory tests, and clinical observations it seemed justifiable to infer that the attacks of hypoglycemia and attending symptoms from which this patient suffered arose from an increased action of insulin. There are two possible mechanisms through which this could occur. It has been demonstrated that both the pituitary and the adrenal cortex elaborate hormones which are insulin antagonists, and it seems possible that a defect in such restraining influences might lead to an unopposed and enhanced insulin effect which could produce severe hypoglycemia even in the absence of demonstrable pancreatic disease or the secretion of grossly abnormal amounts of insulin.

The second possibility involved the actual presence of pancreatic disease. A review of this patient's history discloses the occurrence of diagnostic data which, according to Whipple's criteria, usually designate the presence of adenoma of the islands of Langerhans. An important diagnostic point is that the symptoms provoked by hypoglycemia follow a pattern which is duplicated essentially in all attacks. In a patient who displays a definite pattern of symptoms there is, first, the history of attacks occurring during the fasting state; second, during the attack or after a prolonged fast the blood sugar falls below 50 mg. per cent; and, third, the patient becomes symptom-free immediately on the intravenous administration of glucose. According to Whipple's statistics about 80 per cent of the adults whose disease fulfilled these diagnostic criteria were found to have operable islet tumors.

It was on the strength of this evidence that this patient was subjected to operation, although we knew at the time that typical islet adenomata are practically unknown in children. Nevertheless, since severe and repeated attacks of hypoglycemia can lead to irreversible brain damage, it seemed proper that the patient be given the benefit of every doubt. Accordingly, an exploratory

operation was done. As you have heard, no tumor was found but a partial pancreatectomy was performed. Histologic examination of the removed pancreatic tissue showed considerable hypertrophy of the islets, a condition which duplicates what has been found occasionally in children and frequently in adults who have suffered from severe hypoglycemia. Although no islet tumor was found, it would seem that the great increase of islet tissue would justify the diagnosis of organic hyperinsulinism.

DR. LEVINE.—Are there questions about the diagnosis?

ASSISTANT RESIDENT.—I should like to ask Dr. Schloss whether there is any way of differentiating preoperatively between adenoma of the pancreas and diffuse hypertrophy of islet tissue?

DR. SCHLOSS.—There is apparently no clinical means of doing so. What, if any, is the exact relationship of the two conditions cannot be answered now. It is conceivable that the etiology of the two conditions may be dissimilar despite the fact that they cause identical symptoms. The true adenoma may be a neoplasm while the diffuse hypertrophy could be a response to the stimulative effect of a hormone secreted by another endocrine gland. This would be somewhat analogous to the type of Grave's disease caused by the thyrotropic hormone of the pituitary.

DR. LEVINE.—Now we are faced by the problem of therapy. After the partial pancreatectomy there was apparent improvement, with almost complete absence of symptoms for ten months. As Dr. Schloss has said, the reasons for the operation were first, that without it we could not rule out a tumor, though pancreatic adenomas are admittedly exceedingly rare in childhood; and, second, the danger of mental deterioration as a result of repeated seizures.

The recurrence of the seizures brings up the question of further surgical treatment versus medical treatment. Dr. Schloss, what is your opinion about this?

DR. SCHLOSS.—Reports in the literature of cases in whom successive partial pancreatectomies have been performed have been very discouraging. Dr. Levine, have you ever seen a case where this has finally resulted in a cure?

DR. LEVINE.—Never, in children, where no adenoma has been present.

DR. SCHLOSS.—As for medical treatment, the patient could be treated with alloxan. As you know, this substance causes destruction of the islets and has been used experimentally to produce diabetes in laboratory animals. It has been used in the treatment of humans suffering from hyperinsulinism caused by diffuse islet hypertrophy. Talbot has reported improvement of one patient following its use. This drug, however, is very toxic and can produce severe kidney and liver injury. I think I should prefer to hold it in reserve until more is known of its usefulness and dangers or until all other measures have failed and its employment seems imperative as a last resort. The third course would be to treat the boy symptomatically and this at the moment seems the method of choice. We will give him larger amounts of carbohydrate and at frequent intervals. This regimen has proved useful in similar cases. At the onset of hypo-

glycemic symptoms, which are clearly recognized by his mother, glucose will be given by intravenous injection.

VISITING DOCTOR.—May I ask Dr. Schloss whether he is at all afraid of changing from a high protein to a high carbohydrate diet? Is there any danger in giving too much carbohydrate?

DR. SCHLOSS.—No doubt you refer to the possibility of overstimulation of insulin production. In the functional hypoglycemias such as one sees in adults with no organic cause demonstrable, there is ample evidence that high carbohydrate diet makes them worse. In contrast to this patient, the blood sugar in these functional cases rises after a carbohydrate meal and then makes a sharp drop within one to four hours (usually two to three hours) accompanied by symptoms. This boy's low point in blood sugar comes with prolonged fasting. It would seem that suitable dietary management in this case would consist of frequent small meals of fairly high carbohydrate content, with extra carbohydrate when prodromal symptoms suggest its need, in order to ward off attacks. If he can be kept comfortable and free from severe attacks it is possible that there will be discovered some method of hormonal control of the islet hypertrophy or even a direct insulin antagonist of therapeutic value.

Case 2. Congenital Adrenocortical Insufficiency With Virilism

DR. WARREN TEPPER (Assistant Resident in Pediatrics).—This white male infant, born Oct. 27, 1948, was admitted to the pediatric service of The New York Hospital on November 27 because of vomiting and poor weight gain. His parents were first cousins and of Italian descent. The mother was 28 years old. The pregnancy, except for spotting for one week in the first trimester, and the birth were normal. In the nursery the infant vomited small amounts of formula frequently; this persisted after discharge on the sixth day. At 10 days of age he became cyanotic during bubbling, was admitted to another hospital and put in an oxygen tent. Right-sided tremors were noted and a blood culture was positive for hemolytic *Staphylococcus aureus*. The culture became sterile following a course of intramuscular penicillin in high dosage but the vomiting continued. Lumbar puncture, subdural tap, gastrointestinal series, and barium enema were all negative. A roentgenogram of the chest on the fifteenth day of life demonstrated a left pneumothorax which cleared spontaneously. Two weeks after admission he had another transient episode of cyanosis. Despite a good appetite daily parenteral fluids were required to prevent dehydration. In the week prior to admission to The New York Hospital he had four to six loose, green, foul stools daily which diminished in frequency on a protein milk formula. At one month, he weighed 9 ounces less than at birth and was transferred to The New York Hospital.

Examination revealed an extremely malnourished and dehydrated infant. He was active but irritable and sucked his fists hungrily. His respirations were shallow and rapid. The skin was olive-brown and mottled with fair turgor; the subcutaneous fat deposits were markedly depleted and the skin hung in folds which were particularly prominent along the inner aspect of the thighs. There

was a papular, erythematous, scaly eruption on the scalp. The anterior fontanel was open, 3 by 5 cm., and depressed; the posterior fontanel admitted a fingertip. The abdomen was distended and tympanitic and the liver edge was palpable 3 cm. below the costal margin in the midcostal line. The spleen and kidneys were not felt. The penis seemed comparatively large. The testes were in the scrotum, were of normal size, and had a firm feel. The prostate was not palpable by rectal examination. The extremities were cold and faintly cyanotic. There was no fever or sign of infection. Physical measurements were as follows: weight, 2,820 Gm.; head circumference, 35.5 cm.; chest, 33 cm.; abdomen, 32 cm.; stem length, 35 cm.; total length, 55 cm. His appearance is shown in the first slide (Fig. 2).

Fig. 2.—Photograph of baby taken at 5 weeks of age, Dec. 2, 1948.

Laboratory tests demonstrated a negative urinalysis. The blood counts and differential showed hemoglobin 22 Gm.; red blood cells 6,400,000, white blood cells 7,100; differential: 66 per cent lymphocytes, 4 per cent eosinophiles, 30 per cent polymorphonuclears. On fluoroscopic examination the heart appeared undersized and its transverse diameter was estimated to be one-third that of the thorax.

Chemical examination of the blood on Nov. 27, 1948, showed: potassium 7.9 mM per liter, sodium 130 mM per liter, bicarbonate 20 mM per liter, calcium

TABLE I. MALE INFANT WITH ADRENOCORTICAL INSUFFICIENCY AND VIRILISM

PERIOD			CONCENTRATION IN SERUM*							TREATMENT*					
DATES 1948-1949	DURATION (DAYS)	WEIGHT* (GM.)	SODIUM (mM./L)	POTASSIUM (mM./L)	CHLORIDE (mM./L)	BICARBONATE (mM./L)	PROTEIN (GM./100 ML.)	UREA N (MG./100 ML.)	GLUCOSE (MG./100 ML.)	FLUID PER OS (ML./DAY)	FLUID PARENTERAL (ML./DAY)	ADDED NaCl (GM./DAY)	ADDED Na LACTATE (GM./DAY)	ADRENAL CORTICAL EXTRACT (ML./DAY)	DESOXYCORTICOSTERONE ACETATE (MG./DAY)
11/28-12/1	3	2,580	118	6.3	98	19	7.6	56	36	430	90	0.8	–	–	–
12/2 -12/3	1	2,559	134	4.7	114	15	5.5	–	–	480	260	3.3	–	22	–
12/4 -12/6	2	2,520	119	9.5	101	21	7.6	15	56	560	210	4.9	1.1	11	–
12/7 -12/10	3	2,630	120	7.8	92	30	6.7	–	–	585	330	6.6	2.8	18	2
12/11-12/13	2	2,740	141	5.0	101	23	6.1	–	–	580	270	5.3	0.5	20	4
12/14-12/20	6	2,800	132	6.1	98	29	6.7	–	–	870	–	5.0	0.5	10	4
12/21- 1/7	16	3,760	138	4.9	107	25	4.9	–	–	770	–	5.0	0.5	–	5
1/8 -1/18	10	4,088	132	5.4	107	27	5.4	–	–	710	–	5.0	0.6	–	2
1/18- 1/24	6	4,454	143	5.1	110	27	5.7	–	76	766	–	3.5	0.8	–	2
1/25- 1/29	4	4,479	141	6.3	111	22	5.9	–	88	743	–	3.5	0.8	–	–
1/30- 2/1	2	4,380	135	8.1	107	–	–	–	–	729	–	1.4	0.4	–	–
2/2 - 2/5	3	4,338	140	6.1	104	22	–	14	–	695	–	1.4	0.4	–	2
2/6 - 2/16	10	5,020	138	5.5	108	25	5.6	–	92	723	–	3.5	0.8	–	2
2/17- 2/23	6	5,180	133	5.8	112	–	–	–	–	685	–	3.5	0.8	–	1
2/24- 2/25	1	5,300	–	–	–	–	–	–	–	750	–	3.5	0.8	–	2

*The values for weight, concentration in serum, and treatment are those on the last day of the period stated and represent approximately the values obtaining throughout the period.

10.7 mg. per 100 ml., phosphorus 5.3 mg. per 100 ml., blood urea nitrogen 24 mg. per 100 ml.

The relation of the more important examinations of the serum to the type of treatment given during the three-month period in the hospital is shown on the blackboard (Table I).

Despite the absence of diarrhea and vomiting from November 28 to December 1, it may be seen that a customary food intake with small amounts of parenteral fluids and added salt was associated with a progressive loss of weight and a reduction in serum sodium, chloride, and bicarbonate, elevation of blood urea nitrogen and increasing clinical signs of dehydration and collapse. Large quantities of parenteral fluids and added sodium chloride were started on December 2 and the infant was given 22 ml. per day of adrenal cortical extract. By December 4 the serum potassium had fallen and the sodium and chloride levels had risen but the bicarbonate content was still reduced, there was no weight gain and only slight clinical improvement. Even the chemical improvement was not maintained on this regimen, as shown by the fall of serum sodium to 119 and the rise of serum potassium to 9.5 mM per liter on Dec. 6, 1949. During this period the infant was almost moribund on several occasions. Daily intramuscular injections of desoxycorticosterone acetate in oil in a dosage of 2 mg. were begun on Dec. 7, 1948. This was increased to 4 mg. daily on December 10 and by December 14 on this dosage of desoxycorticosterone acetate combined with 20 ml. per day of adrenal cortical extract, 5 Gm. of added sodium chloride, 0.5 Gm. of sodium lactate, and total fluids up to quantities of 350 ml. per kilogram, chemical control and real clinical improvement occurred. The latter was manifested by disappearance of the signs of dehydration, improvement in peripheral circulation, and by the general appearance of the infant. During the period from December 14 to December 20, parenteral fluids were discontinued and the adrenal cortical extract was progressively decreased from 20 ml. per day until it, too, was discontinued, at which time the dosage of desoxycorticosterone acetate was increased from 4 to 5 mg. The infant showed rapid progress with marked weight gain during this period. On Jan. 8, 1949, the dosage of desoxycorticosterone acetate was decreased to 2 mg. daily and on a customary formula with the addition of 3.5 to 5.0 Gm. of sodium chloride and 5 to 7 ml. of molar sodium-r-lactate, the infant continued to thrive. Between January 25 and February 1, when desoxycorticosterone was withdrawn and the amount of added sodium decreased, the infant again lost weight and showed signs of dehydration and poor peripheral circulation associated with a slight but significant fall in serum sodium and a rise in serum potassium. As shown in the table, these changes were again reversed on resuming injections of desoxycorticosterone acetate and increasing the amount of added sodium. During the period of February 17 to 23, when the dosage of desoxycorticosterone acetate was reduced to 1 mg. daily, there was no striking change in the serum chemistry but the infant was less active, ate poorly, gained weight more slowly, and looked less well. Increasing the daily dosage to 2 mg. on February 24 was again associated with clinical improvement.

(The infant was brought in. See Fig. 3.)

DR. S. Z. LEVINE.—You can see that at 4 months this baby appears healthy and well nourished. The contrast with his appearance on admission, as you saw it in the photograph, is striking. The testes feel firm though not large. Recently, long, fine dark hair has appeared on the side of the face down to the level of the mouth. Although this is not more than is seen in some infants with no virilism, it is unusual in that it appears to be increasing rather than decreasing.

Dr. Tepper, has a recent rectal examination been done?

DR. TEPPER.—Yes, sir, by Dr. Barnett.

Fig. 3.—Photograph of baby taken at 4 months of age, Feb. 24, 1949.

DR. HENRY L. BARNETT (Assistant Professor of Pediatrics).—I palpated a suggestive mass in the region of the prostate.

DR. LEVINE.—Are there questions about the story so far, before the infant is taken out?

VISITING DOCTOR.—Was any other therapy given besides that described?

DR. TEPPER.—Yes. During this extended period the infant received several blood transfusions and was given penicillin and aureomycin for short periods because of mild respiratory infections. He received various forms of evaporated milk formulas, added vitamins A, C, and D, and at 3 months was started on solid foods. There has been no indication that these measures or any factors other than those shown in the chart had any specific influence on the progress of the infant.

VISITING DOCTOR.—What other laboratory studies were made?

DR. TEPPER.—Repeated electrocardiograms showed changes which correlated with and were interpreted as being due to changes in potassium. These changes included elevation of the T wave during periods of hyperpotassemia and a decreased voltage in all deflections during periods of desoxycorticosterone acetate injection. Determinations of 17-ketosteroids for two twenty-four hour periods, done in Dr. Ephraim Shorr's laboratory, showed 3.78 and 5.70 mg. per twenty-four hours. Injection of 8.5 mg. of adrenocorticotropic hormone showed no decrease (patient: plus 1 per cent, control: minus 89 per cent) in circulating eosinophiles and no significant increase (patient: plus 10 per cent, control: plus 65 per cent) in the uric acid-creatinine ratio after four hours. He was given the Cattell Infant Intelligence scale at the age of 3½ months by Miss Elizabeth New. He scored a mental age of 4 months which is slightly ahead of his chronological age and seems to indicate that at the present time his intellectual development is on the high average level.

Roentgenograms demonstrated no intra-abdominal masses or calcification, and bone age was interpreted as within normal limits. Repeated blood counts have been within normal limits except for an unexplained eosinophilia and relatively high percentage of lymphocytes.

DR. LEVINE.—At the time of admission, the appearance of this infant was characteristic of the type of severe malnutrition and dehydration in a one-month-old infant which could have been produced by a variety of conditions. It soon became apparent, however, that the underlying cause for the failure of this infant to thrive was an unusual one, and even after it was determined, the proper course of treatment presented many problems. Dr. Barnett, Miss McNamara, Dr. Hare, and their group have just completed an extensive series of observations directed toward elucidating some of the problems involved, and Dr. Barnett will discuss this patient and describe some of their results.

DR. BARNETT.—When seen here at one month of age, this infant presented certain unusual features which led Dr. Mosher first, I believe, to suspect that he might be suffering from adrenal insufficiency. His failure to thrive, the episodes of collapse, and the extreme degree of dehydration and anhydremia were not adequately explained by the history and findings. The probability of this diagnosis being right was increased when the serum was found to contain a high level of potassium and a low level of sodium, and further, by failure of large quantities of water and sodium to correct these chemical changes and the dehydration even in the absence of diarrhea or vomiting. His subsequent dramatic response to desoxycorticosterone acetate and added salt, the reappearance of the symptoms and findings with their withdrawal and the absence of response to adrenocorticotropic hormone, all served finally to establish the diagnosis of adrenal insufficiency. Although his penis is relatively large and there appears to be beginning abnormal growth of facial hair, these two possible manifestations of virilism are not definite enough to be certain that they do not represent normal variation. However, the urinary excretion of 4.7 mg. of 17-ketosteroids per twenty-four

hours is elevated to the level normally found by Talbot and associates[1] in prepubertal boys so that enlargement of the penis, growth of facial hair, deepening of the voice, acne, excessive growth and muscular development, and epiphyseal closure are expected to occur precociously. It seems clear, then, that this boy has the type of adrenal disease first recognized and described in 1939 by Butler, Ross, and Talbot[2] and by Wilkins, Fleischmann, and Howard,[3] in which there is insufficiency primarily of the electrolyte controlling hormone or hormones and an excess of the androgenic hormone of the adrenal. Thelander and Cholffin,[4] Bratrud and Thompson,[5] and Darrow,[6] have described additional infants with this syndrome and although many aspects of it remain unclear, certain concepts have emerged. In all instances in which the adrenals were examined, bilateral hyperplasia was found. This type of hyperplasia is recognized more frequently in girls in whom it produces pseudohermaphroditism. It is of interest, however, as pointed out recently by Wilkins,[7] that of the eighty-three reported cases of female pseudohermaphroditism due to congenital hyperplasia, associated adrenal insufficiency is known to have occurred in only six, whereas of sixteen males with the same disturbance, ten had evidences of such insufficiency. It seems possible that the apparent greater incidence of congenital bilateral adrenocortical hyperplasia in females may stem from the fact that pseudohermaphroditism is apparent at birth and is less frequently associated with adrenal insufficiency whereas in boys virilism is not manifest at birth and many may have died from the more frequently associated adrenal insufficiency before virilism had appeared and, therefore, without being recognized as adrenocortical hyperplasia. A further important fact to be learned from the reported cases of adrenal insufficiency with virilism is that in well over one-half of them congenital adrenocortical hyperplasia occurred in other siblings, manifesting itself by similar findings in brothers or pseudohermaphroditism in sisters.

I should like to point out some features of the condition exemplified by the infant we are presenting today. From the table it may be seen that despite an initial response to adrenal cortical extract with added intake of sodium chloride, sodium lactate, and large amounts of fluid, persistent control of the signs and symptoms of insufficiency was achieved only after a relatively enormous dosage of desoxycorticosterone acetate was additionally given. Once the insufficiency had been controlled, much smaller doses of all the therapeutic agents were effective. At one point in the course of treatment of this patient when both desoxycorticosterone acetate and adrenal cortical extract were being given, decreasing the amount of adrenal cortical extract from 20 ml. to none had little if any discernible effect, whereas during a subsequent period when he was receiving no adrenal cortical extract, decreasing the dosage of desoxycorticosterone acetate from 2 mg. to none and even from 2 mg. to 1 mg. produced a striking change. We cannot, however, assay the relative potency of the two compounds in controlling water and electrolytes in this patient from these observations since adrenal cortical extract was probably being given in excess of the patient's needs when it was decreased, whereas when the dosage of desoxycorticosterone was decreased he was close to his minimal requirements for exogenous electrolyte and water controlling hormone. At no time during the period when he was receiving

such enormous dosages of desoxycorticosterone acetate did he show roentgenographic evidence of cardiac enlargement or clinical edema which would suggest overdosage of the hormone. At the present time, at the age of 4 months, the patient seems to be well controlled on the regimen described, which consists of a regular infant diet with 3.5 Gm. of sodium chloride and 0.8 Gm. of sodium lactate added to the formula and the daily intramuscular injection of 2 mg. desoxycorticosterone acetate in oil. From Darrow's observations,[6] we have considered the advisability of including the addition of potassium chloride to this regimen. However, from data derived from detailed observations on his electrolyte balances with varying intakes of sodium, chloride, and potassium, which are reserved for later publication, it appears that he does not need potassium in excess of the amount he is receiving in his milk.

DR. LEVINE.—Would you be willing to venture an opinion as to the prognosis, Dr. Barnett?

DR. BARNETT.—The number of cases in which this abnormality has been diagnosed before death and in whom follow-up observations were made is so small and the progress of the few who have been followed varies so greatly that no reliable prediction concerning this patient's future is possible. From what we do know, the prognosis is not very hopeful. The patient described by Butler, Ross, and Talbot[8] in 1939 is still alive at the age of 11 years and shows persistence of his water and electrolyte disturbance, deep pigmentation, extreme virilism, and dwarfing. Thelander's patient[9] died at 6 years with measles. His need for hormone had also persisted and extrapolation of his rate of growth suggested that his ultimate height would have been below average. The poor response to infections suggested in this patient has been apparent in others. Darrow's patient[10] died at about the age of 4 years and showed diffuse enlargement of the adrenals and an enlarged heart. The patient reported by Wilkins, Fleischmann, and Howard[3] died at 3½ years of age when an excess salt intake was inadvertently interrupted.

VISITING DOCTOR.—May I ask Dr. Barnett about the effect of this severe metabolic disorder on mental growth? It has been stated that at present the patient's mental age is normal or above. If he survives, what is his prognosis in this respect?

DR. BARNETT.—The children reported by Butler, by Darrow, and by Wilkins showed definite evidence of mental retardation. Thelander's patient, on the other hand, exhibited normal mental development, and with psychiatric help and through an intelligent attitude of everyone concerned, including not only the parents but neighbors, nursery school teachers, and others, he did very well in his emotional adjustment.

The difficult emotional adjustment which confronts this patient and his family presents a problem of equal magnitude to that posed by his metabolic difficulties. The problem has been approached initially by the pediatrician, taking advantage of the relationship which has already been established. An attempt is being made to help the parents to accept first intellectually and then

emotionally the baby's differences from other children. Since his differences will be primarily sexual manifestations, their own attitude toward sex must be examined in order for them to face realistically their emotional reaction to the child. At a later time the family may need the help of a fully trained psychiatrist, and the present role of the pediatrician is to prepare them for this. The question of future pregnancies has been discussed and the occurrence of similar disorders in siblings described. This was done after considerable preparation and did not appear to be too immediately disturbing. No pregnancies are contemplated for the next year or two, during which time there will be opportunity for further discussion.

DR. LEVINE.—It seems clear at the present time that there are at least three distinct functions of the hormones of the adrenal cortex. Desoxycorticosterone acetate is at least one of the hormones which controls water and electrolyte excretion, and we have adequate evidence of such insufficiency in this patient. The 17-ketosteroids are among the hormones responsible for the development of some of the secondary sexual characteristics, and the increased urinary excretion of this hormone in the urine and the clinical suggestions of beginning virilism are strong evidence for an excess of this hormone. Hyperplasia of the androgenic cells may actually be responsible for failure of the other cells to function. Are there any evidences of disturbance in the 11 oxysteroids, which are concerned with sugar-fat-nitrogen metabolism?

DR. BARNETT.—Evidence for sugar-fat-nitrogen hormone deficiency has not been prominent in the reported cases. Our patient's episodes of cyanosis and collapse during the first month of life could have been due to hypoglycemia. This suggestion is strengthened by the finding of a blood sugar value of 36 mg. per 100 ml. here. However, there have been no further evidences of disturbance in this area, so that it seems likely that either he has none or that it is of such a slight degree that regular feedings would be sufficient to prevent periods of hypoglycemia. I would suspect that he might not tolerate prolonged periods of fasting well.

VISITING DOCTOR.—Were there changes in blood pressure during the periods of varying control?

DR. BARNETT.—There did not appear to be. There were at least no periods of definite hypotension or hypertension that could be correlated with his changing status.

VISITING DOCTOR.—Is there any possibility of the signs and symptoms of adrenal insufficiency in this infant disappearing so that later he will not require hormone and added salt?

DR. BARNETT.—In the last few years Dr. Jaudon of St. Louis has emphasized a syndrome characterized by nausea, regurgitation, vomiting, eventual dehydration, and collapse, accompanied by excessive renal loss of sodium chloride and water. He attributes the cause of the syndrome to a temporary absence or a physiologic low supply of the electrolyte and water-controlling hormone of the

adrenal glands, and has presented evidence[11] to demonstrate that adrenal cortical hormones and salt are of specific therapeutic value in these infants. In these infants, therapy can eventually be discontinued and there has been no laboratory or clinical evidence of virilism. We have not seen any infants here who we thought belonged in this category and although Jaudon's evidence for the existence of such a syndrome is suggestive, we cannot accept it unqualifiedly. Of the patients who have shown adrenal cortical insufficiency associated with virilism, the need for continued therapy with desoxycorticosterone, salt, or both has persisted in all instances and this is what we must expect, therefore, in this infant.

DR. LEVINE.—We expect to see this patient at frequent intervals and will hope to present him for a follow-up at some future date.

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Case 3. Cholelithiasis in Childhood

DR. LEVINE.—The third child on our list today has been discharged. We present her case not as a diagnostic or therapeutic problem, but because it illustrates a surgical condition which is relatively infrequent in childhood.

DR. SARAH MATTESON (Intern in Pediatrics).—B. G., a 5½-year-old white girl of Italian parentage, was admitted to the New York Hospital in December, 1948, with the complaint of recurrent abdominal pain since the age of 3 months. With the introduction of solid foods to the diet, she began to have attacks of abdominal pain associated with nausea and vomiting. Until 3 years of age the episodes occurred once or twice a month. From then until the time of admission to the hospital the attacks became more severe and occurred two to three times a week. Each lasted about two to three hours and was accompanied by nausea and vomiting. The mother stated that the pain seemed to be related to the eating of fatty foods. No jaundice was noted. On a low fat diet the severity and frequency of the attacks diminished. However, the patient repeatedly com-

plained of a dull ache in the abdomen, usually on the right side, which remained more or less constant between the acute episodes. Plain roentgenograms of the abdomen at 4 years of age revealed calcific densities in the right upper quadrant which were interpreted as gallstones.

On admission, the positive physical findings were voluntary spasm and questionable slight tenderness to deep palpation in the right upper quadrant, and a smooth, nontender liver edge palpated 1 cm. below the right costal margin.

Laboratory studies including complete blood examination, liver function tests, and sedimentation rates, revealed no evidences of a hemolytic anemia, infection, or liver disease.

DR. LEVINE.—Before we hear about what was found and done at operation, I shall ask Dr. Dale to present the x-rays (Fig. 4).

DR. JOHN H. DALE, JR. (Assistant Professor of Pediatrics in Radiology).—Oral cholecystography showed a well-filled gall bladder which appeared normal in size, shape, and position. There were two calcific densities in the fundal region and another ovoid density in the region of the cystic duct. Examination of the gastrointestinal tract revealed an elongated, narrowed, pyloric canal with evidences of retention of the barium meal. The duodenal swing was wider than usual. It was thought that there was moderate pylorospasm and possibly enlarged lymph nodes in the region of the head of the pancreas accounting for the widened duodenal loop.

DR. LEVINE.—Does anyone have any questions before Dr. Matteson goes on with the description of the operation and subsequent course?

DR. MATTESON.—At operation, the gall bladder was exposed and found to be thickened and edematous but not inflamed. The gall bladder was adherent to the second portion of the duodenum, accounting for the widened duodenal swing. The structures within the loop of the duodenum were normal. External examination of the gall bladder failed to reveal any evidence of a cystic duct. On opening the organ, two green stones were found in the fundus. The cystic duct seemed to be almost lacking and was represented by a few mucosal folds simulating the valves of Heister. Caught within these folds was a long, spiral-shaped gallstone. The gall bladder appeared to unite directly with the common duct. No calculi were found in the latter. The gall bladder was removed. The pathologic report was "chronic cholecystitis with cholelithiasis."

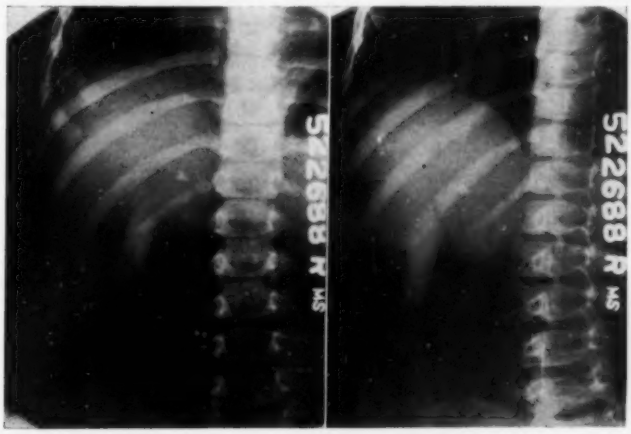
Recovery was uneventful and the child was discharged ten days after operation. Follow-up during the past two months has revealed a complete freedom from all previous symptoms.

DR. LEVINE.—I am sorry we do not have this patient here, but when last seen she showed no positive findings except for her healed abdominal incision. The liver was not enlarged. I will call on Dr. Dale to discuss cholecystitis and cholelithiasis in childhood.

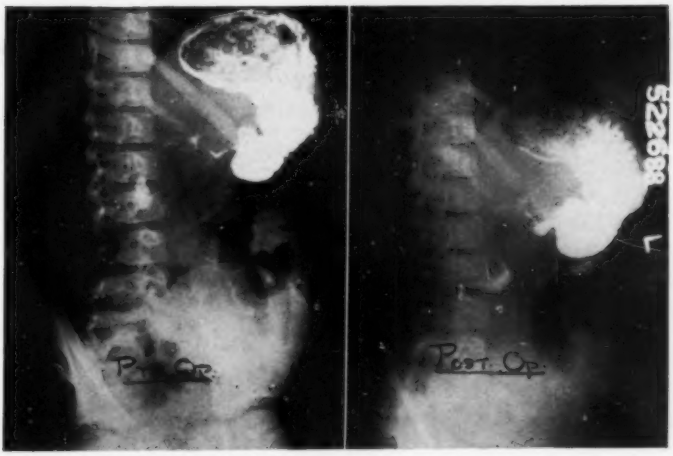
DR. DALE.—Gall bladder disease in childhood has been considered to be rare. The diagnosis is seldom entertained and many cases are diagnosed only at the

time of operation for some other intra-abdominal condition or at autopsy. In 1938, Potter reported a total of 432 cases of gall bladder disease in children collected from his material and from the literature. Of these, 306, or approximately 70 per cent, had cholelithiasis. Ladd and Gross state that cholelithiasis is far more common in childhood than acute cholecystitis.

The symptoms are similar to those noted in adults but are less well localized. Referral of pain to the shoulder or the back is not the rule in children. The chief symptoms are periumbilical or right upper quadrant pain associated with



A.



B. *C.*

Fig. 4.—*A*, Oral cholecystography demonstrating the presence of gallstones and the stone in the cystic duct. *B* and *C*, Preoperative and postoperative changes related to the pylorospasm, and widened swing of the duodenum, shown at operation to be secondary to adhesions between the gall bladder and the duodenum.

nausea and vomiting. There is usually fever. Physical examination may reveal tenderness in the right upper quadrant associated with spasm. Occasionally the distended gall bladder may be palpated below the right costal margin. In young children the condition is usually diagnosed as acute appendicitis. The diagnosis of gall bladder disease in childhood is best made by oral cholecystography.

Most authors are in agreement that the majority of cases of gall bladder disease in children are attributable to congenital anomalies of the biliary system, systemic infection, upper respiratory infection, infection of the gastrointestinal tract, or to parasitic infestation. The fact that the incidence of gall bladder disease has not decreased with the lowering of the incidence of typhoid fever suggests that there has been overemphasis of the importance of the latter in the production of gall bladder disease. Cholelithiasis is frequently associated with the congenital hemolytic anemias. In fact, the presence of gallstones should alert the clinician to the possibility of the existence of one of this group of anemias. Cholelithiasis may result from biliary stasis secondary to malformation of the extrahepatic biliary system, from infection of the gall bladder, spasm of the ampulla of Vater, extrinsic pressure of enlarged lymph nodes on the common duct, or from inflammation of the common duct. In this case, it would seem probable that the malformation of the cystic duct was the responsible factor in the production of the infection and the gallstones.

The treatment of choice is operative. If there is no evidence of infection, as is the case in the hemolytic anemias, the stones may be removed and the organ left in place. If infection is present, cholecystectomy is the operation of choice.

VISITING DOCTOR.—Was there anything unusual about the composition of the stones?

DR. DALE.—The gallstones removed in this case were composed chiefly of bilirubin, the most common type of stone found in gall bladder disease in childhood.

Psychologic Aspects of Pediatrics

PSYCHOSOMATIC ILLNESS IN CHILDHOOD

A Report of Six Cases

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PSYCHOSOMATIC illness mimics so closely the symptoms of organic disease that its recognition as a clinical entity is an important advance of modern physical diagnosis. Case reports for the most part have emphasized psychosomatic illness in the adult. Recent statistics compiled at the Lahey Clinic[1] showed that in 27 per cent of 1,000 consecutive adult medical admissions complaints were of nervous and mental origin only. In another 13 per cent of these patients organic and functional symptoms were combined. Such reports have prompted us to examine our pediatric records.

A new awareness of functional disorders is demonstrated in the medical service of the Children's Hospital of Pittsburgh. In 1941 the diagnosis of "psychosomatic illness" was made in only twenty-eight cases of 2,068 medical admissions. However, during the past six months, from an admission census of 1,328 patients, our medical records describe twenty-four cases of uncomplicated psychosomatic disease in children. These statistics do not imply a new trend in childhood illness but rather indicate a change in our evaluation of the pediatric patient.[2]

EVOLUTION OF PEDIATRIC PSYCHIATRY

It is not a purpose of this paper to trace the growth and development of pediatric psychiatry. This has been described elsewhere by Kanner,[3] who has reviewed in detail the evolution of child mental health programs. Today certain factors still complicate the approach to psychosomatic illness in the child. For example, the acceptance of such a diagnosis as behavior problem is difficult for parent and physician alike. Arriving at this diagnosis by the usual methods of exclusion of organic disease is expensive. Correction of the inorganic complaints, employing the crude techniques at our command, may be tedious and at times quite unsatisfactory. These difficulties constitute the growing pains of pediatric psychiatry.

APPROACH TO THE EMOTIONALLY DISTURBED CHILD

To the clinician, paradoxically, failure to recognize organic disease seems a far more serious oversight than neglect of a behavior problem. Why should this be? There are certain fundamental emotional demands in this age period.

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No description, however graphic, portrays so well the innermost emotions of a group as does the child who mirrors without distortion all conflicts within the family. Reflected in the emotional outlook of the pediatric patient is an image of the good or bad home environment.

Primary causes of misbehavior include personality oversensitivity, conflicts with home influences, problems of growth and development, pressure of education, and the frustration of instinctive drives.[4] Some combination of these often represents the uncertainties which bring the functionally imbalanced child to the physician.

NOMENCLATURE AND DIAGNOSIS

We have preferred to leave the distinct classification of our cases to the psychiatric consultant. The Committee on Statistics of the American Psychiatric Association has classified the usual psychoneuroses into six separate types: hysteria, psychasthenia, hypochondriasis, anxiety state, neurasthenia, reactive depression (a simple situational reaction), and a mixed group. These diagnoses are readily applicable to the cases presented below. Diagnostic techniques may be simplified also. The first step is elimination of all possible organic foci of disease. Next an evaluation of emotional influences is necessary. Finally there is formed a diagnosis which classifies the etiology of the illness rather than the child.

DIRECT AND INDIRECT THERAPY

The clinician who follows a scheme of systematic analysis should be able himself to evaluate, diagnose, and initiate therapy in the majority of cases. Adjustment of the child rather than mere elimination of symptoms is his primary aim.[5] With the family he approaches directly the genesis of the child's behavior problem. The community provides the indirect social, economic, and religious agents necessary for readjustment of distorted family relationships. Where the psychoneurosis is of serious consequence or where organic mental illness is a factor, only the child psychiatrist is equipped to direct patient guidance. For these refractory cases clinics affording specialized therapy are available.[6]

CASE PRESENTATIONS

We present five cases selected from among fourteen children, diagnosed as uncomplicated psychosomatic problems, admitted to the medical service of Children's Hospital of Pittsburgh between May and September, 1948. The sixth case presented is taken from our outpatient department records during this period. These patients range in age from 2 to 13 years. Each illustrates bizarre behavior patterns which are characteristic of childhood psychosomatic illness.[7]

CASE 1.—The first case is described in some detail to illustrate its far-reaching ramifications of social, economic, and religious significance.

L. W., a 10-year-old white girl, was admitted July 29, 1948, with a chief complaint of daily attacks of sharp, substernal pain lasting one-half to two hours.

Past Medical History.—The mother stated the child had been "sensitive" since birth. A 2-month premature infant weighing 5 pounds at birth, L. had "practically lived on whiskey" for the first five months of her life. The child began to speak at 12 months and walked at 17 months. The past medical history was negative for acute infectious or chronic disease. From July 20 to July 27, 1948, the child had been a patient at a local hospital where only a few attacks had been modified by phenobarbital sedation. Because she was "an unmanageable neurotic" she was discharged.

Family History.—The father, aged 32 years, was a hard-drinking coal miner in good health. The mother, aged 28 years, described herself as "nervous." She suffered frequent palpitations of the heart and complained of chronic fatigue. There was no history in the family of mental disease or chronic illness.

Present Illness.—The attacks began one month prior to admission; they were manifested by substernal pains of crushing nature which the patient stated "cut off my breath."[8] Such attacks, occurring between 7 P.M. and 1 A.M., had been noted on all but six nights in the past month, lasted from one-half to two hours, and left the child completely exhausted. During an attack the mother would hold the child, who was extremely emotionally upset, and often would cry with her, advising her "to scream and get the poison out of her system." As the outbursts became more prolonged the child would gag and vomit mucus; the mother would then give her small amounts of whiskey, which partially relieved her. Following a typical attack the child would fall into a deep sleep.

Such episodes occurred always in the absence of the patient's father, either while he was working on the night shift or out "at the club." The child could foretell an attack a few minutes before its onset; she had never bitten her tongue or been incontinent in an attack.

Physical Examination.—The patient was asthenic, pale, and tense; she did not appear acutely ill. Physical examination was negative except for a generalized hyperrefléxia and a nervous tenseness of the abdominal wall on palpation.

Laboratory Studies.—X-rays of the chest and gastrointestinal tract, as well as cholecystogram, electrocardiogram, electroencephalogram, and pneumoencephalogram were essentially normal. Routine urinalysis, complete blood count and sedimentation rate, serology, and spinal fluid examinations were all reported normal.

Course in the Hospital.—A fat-free diet was prescribed for the child at the time of her admission. Psychiatric interviews were arranged.

Attacks in the Hospital.—During the first week of hospitalization the child had nightly seizures of which the following, a description of the attack occurring at 7 P.M. on the day of admission, is typical:

The patient first began to complain loudly of left-sided chest pain. When seen by the house physician she was clasping her heart and rocking back and forth in bed, moaning loudly. After a few minutes she began to gag and

choke, spitting up a considerable quantity of frothy mucus. Examination disclosed her blood pressure during the attack to be 78/56; normal sounds were auscultated over the heart. The apical rate was 88 per minute. Peristalsis was normal and there was no muscle splinting over the abdomen. The chest was clear to auscultation. There was no tenderness elicited on pressure over the xiphoid process nor did pressure on the ribs modify the pain.

The patient had had a slice of toast and a glass of skimmed milk immediately preceding the attack but did not vomit stomach contents. At one time during the attack she requested whiskey "which helped me at home." The attack was relieved by a hypodermic of sodium phenobarbital and the patient dropped off into a deep sleep.

Therapy.—During the first week attacks were controlled by sedatives, while the child was evaluated clinically and organic disease ruled out as carefully as possible by the tests described above. Mild suggestion to the patient that some relief might follow the x-ray studies did not alter the pattern of her attack.[9]

After completion of the negative studies, psychotherapy was begun. At first L. was told that she would not be sent home until her attacks had ceased. Rapport was established after several interviews and aeration of her views on home conflicts was encouraged. After she had been reassured that family troubles would be cleared up her personality changed; she became cheerful, alert, and helpful. She was rewarded for improvement by assignment as helper in caring for a few of the younger patients on the ward. She responded well to this treatment and remained free of attacks from Aug. 7, 1948, until her discharge on August 12.

Social Service Investigation of the Patient.—The patient had good relationships with teachers, friends, and neighbors, as well as her sisters. She had always been shy and reticent and her intelligence was estimated to be above normal for her age.

First Social Service Interview With Mother.—During the interview the mother manifested many nervous complaints and stated that she often felt ill and nauseated "just like L." The mother described the father as drunk and abusive to her and to the children. He gambled heavily and they had quarreled frequently. Although in the past he had seldom struck the children, he often threatened to choke them "if they didn't keep quiet." However during the week prior to L.'s admission, the father had beaten the younger son (aged 8) several times. The boy had run away from home on two of these occasions and the mother said he, too, was a problem child.

The mother stated the patient seemed to fear the dark, to fear storms and loud explosions, and to fear that the father would choke her mother or herself.[10] She frequently lay awake at night asking repeatedly whether her father would come home drunk. The mother stated that she was unable to divorce the father because of their religious belief, but she only "tolerated him for the sake of the children."

Social Service Interview With Father.—Although evasive in his answers early in the interview, the father at length stated that perhaps several quarrels with his wife in the presence of the patient had made the child nervous. He said he had never touched L., but had once or twice threatened her. He confided that he had drunk and gambled during the early years of his marriage, but in the past two years, realizing his family life was insecure and the home atmosphere was bad for the children, he had tried to stay sober and stop squandering money. He felt that his wife would not forgive him for past grievances and would not help him in the attempt to create a good family life. For three months she had refused to sleep with him, and occasionally she would not speak to him for several days at a time.

At the conclusion of the interview it was suggested to the father that the mother and children were fearful of abuse and were frightened by lack of security in the home. With this simple explanation as the probable source of the child's illness the father agreed to cooperate in changing the family atmosphere, to show concern for his wife's poor health, and to discipline his own habits.

Second Social Service Interview With Mother.—During the second interview the mother was encouraged to be more tolerant of the father in his attempt to reform, to forget past grievances, and to seek encouragement from the local social service counsellor, who was given a summary of this case. She was reassured about the prognosis of the illness of her problem children. She was also offered the service of a medical clinic for evaluation and treatment of her personal health problem. Finally, she was urged to seek the advice of the local priest whom she trusted and had known since childhood.

Disposition of the Case.—The social service worker in this family's community was given responsibility for rehabilitation of the patient and her family. It was her report on family conditions, undertaken at the referring physician's request, which had focused attention on important environmental factors in the case.

The referring physician was sent a detailed summary of the case. He assumed responsibility for medical care of the family.

The local priest, who showed great interest in the case, undertook the program of spiritual guidance which has ultimately proved most efficacious in resolving many of the parents' differences.

CASE 2.—Our second case, seen in the outpatient department of the Children's Hospital in September, 1948, illustrates still another type of psychosomatic problem. In this instance a chance remark of the parent led to the uncovering of a whole series of difficult family conflicts.

L. M., a 5-year-old white girl, was examined on Sept. 19, 1948. Her chief complaint was anorexia and vague abdominal pain, and sore throat of twenty-four hours' duration. Past medical history was essentially negative.

Family History.—The mother, father, and a sibling aged 15 months were all living and well. There was no family history of chronic disease. The mother, aged 24, was a college graduate. The father, aged 30, was an office clerk with a high school education.

Present Illness.—During the past month the child had manifested anorexia with slight, generalized abdominal pain occurring always during or immediately following the evening meal.[11] These symptoms became aggravated at the child's bedtime, and she often stayed awake demanding sympathy until her father had gone out for the evening. The child would fall asleep after his departure. She had never vomited or gagged, but showed her discomfort by groaning and whimpering aloud. Her bowel movements were regular and she had no urinary complaints. She had developed a mild upper respiratory infection one day prior to her visit to the clinic; this was the primary concern of the mother.

Physical Examination.—The patient was intelligent, talkative, well developed and well nourished; she did not appear acutely ill. Positive physical findings included a nasopharyngitis and a few excoriated areas about the labia and rectum.

Additional Information.—Because of the peculiar pattern of the above complaints, the mother was questioned more closely when the physician had finished his physical examination of the child. The parent stated that she believed the patient resented any affection of the father for the mother or the patient's sibling. The child would greet the father as he returned from work just before supper with the announcement, "I've been sick all day." This would provoke him to accuse the mother of neglecting the child and thus set the stage for several family arguments in the course of an evening. L.'s symptoms of anorexia and abdominal pain would begin if the father did not feed her or hold her on his lap during the evening meal. These complaints were aggravated by any attention the father might give the mother or sister during the remainder of the evening.

The mother said that since the birth of her younger child the husband usually went out every evening, sometimes not returning home at all. She confided that she and her husband had not been sleeping together since her last pregnancy. She added that when the father did sleep at home, the patient would insist upon sleeping with her mother. The mother commented that she felt all this was because the child "knew too much" and "was jealous" of her mother, as well as her sister. She said her husband accused her of not loving L. as well as her sister, and was flattered by the child's demonstrations of affection. As a result, he neglected the younger sister.

The patient was given a prescription for her cold and the mother was admonished to return with the child to the Neurology (Behavior) Clinic the next morning.

Social Service Follow-Up.—The mother failed to keep the appointment at the Behavior Clinic. A social service worker was asked to interview the family. The mother was telephoned but was unable to make an appointment for an interview at the hospital. She reluctantly agreed to a home visit by the social worker.

First Social Service Interview With Mother.—The mother said the family had moved to Pittsburgh twenty months previously, but had not made any new acquaintances. She eagerly confided that the patient was a masturbator; she had noted this first when she had returned from the hospital with the new

baby. L. was described by the mother as rubbing her thighs and genital areas to stimulate herself, working up a perspiration and seeming to achieve climax.[12] The child had told the mother she had seen her aunt doing this. The aunt had cared for the patient while the mother was at the hospital.

Prior to the time the mother had gone to the hospital the child had slept in the same room with her mother and father. When in the fifth month of her second pregnancy the obstetrician had restricted the mother's sexual activity, the father had suggested the mother and L. sleep together in a bedroom separate from him. During the past fifteen months the mother had been unable to change this arrangement. The baby slept alone in a crib in another bedroom, for L. refused to sleep on the cot provided for her there.

The social worker observed that the 15-month-old sister was obviously her mother's favorite.[13] All play centered about the baby, and if the patient tried to play with her sister's toys, she was immediately disciplined by her mother. This would provoke a stormy family scene.

Second Social Service Interview With Mother.—A second home interview was held on Sept. 23, 1948. At this time the mother questioned whether she might regain her husband's attention by taking a position in the office with him, leaving the children in the care of a nursemaid. It was pointed out to the mother that her duty was gradually to break L.'s habit of sleeping in her bed, and to turn her attention from sexual abuse. The mother was horrified at the suggestion that she might take the first step toward renewing relations with her husband. The social worker attempted to persuade her to seek advice from the local Child Guidance Center. Despite frequent follow-up attempts by the social agencies and the center the mother continued to disregard the problems of her child, refusing further interviews or counsel and stating she was "sorry she had ever begun this business."

Disposition of the Case.—Unfortunately, we have as yet no means of enforcing our prescription for psychotherapy in cases such as the above. The unsatisfactory disposition of the case illustrates well the resistance of a modern family to even the most tactful attempts at psychiatric guidance. Such an attitude constitutes a very real obstacle in pediatric psychiatry today.

CASE 3.—This case demonstrates thorough study of a typical behavior problem.[14]

F. H., a 28-month-old white female child, was admitted Aug. 30, 1948, with a chief complaint of temper tantrums and hyperactivity of two months' duration.

Past Medical History.—This disclosed a normal birth and developmental background. The patient had been painstakingly trained in her bowel habits by the age of 10 months. There was no history of acute infection or chronic disease.

Family History.—There were no siblings. The mother, aged 27, had had two years' training as a nurse; she complained of bad nerves. The father, a pharmacist aged 28 years, was in good health. There was no history of organic familial disease.

History of the Patient's Illness.—The patient had always been restless and unmanageable, but the mother had noted a decided change for the worse in the child's conduct during the past two months. At this time the family had moved into a new two-story apartment and F. had refused to sleep in her new room or bed on the second floor. The child insisted instead that she sleep downstairs on the couch near her parents. She often picked up dirt, cigarettes, or grass and ate them, even though she was spanked severely for such actions. When spanked she became completely wild; when confined to her room for punishment she would scream at the top of her lungs, often for as long as one or two full hours.[20]

Physical Examination.—The patient was well developed and well nourished, uncooperative and irritable; she resisted the examination with screams and several times attempted to bite the examiner. There were no unusual physical findings. A thorough neurological examination revealed no abnormalities.

Laboratory Studies.—Blood and urine studies, serologic examination, sedimentation rate, and chest x-ray were all reported as essentially normal. Studies for heavy metal poisoning were negative. Therapeutic vitamin therapy with moderate sedation had little effect upon the tantrums. Two psychometric tests (Cattrell and Merrill-Palmer) given at this time showed the child to have a mental age of about 22 months, interpreted by the psychologist to reflect neglect of the patient's abilities by her parents.

Course in the Hospital.—Because parental visits precipitated loud outbursts, the family was requested not to visit the child. The mother retaliated by having the child moved to a private room where she might exercise unlimited visiting privileges. Despite large doses of phenobarbital and reassurance by the nurses, F. was completely unmanageable, passing from one tantrum to another whenever she was left alone. These outbursts were characterized by crying, lusty screams, and sustained physical activity.

Finally on Sept. 3, 1948, her parents were prevailed upon to return the child to a ward with children of her own age. By September 7 the patient was much improved. She had had no further tantrums and was responding well to the affection of the nursing staff. She had begun to play with her fellow patients and demonstrated an alert mind and pleasing temperament.

At the time of her return to the care of the referring physician on Sept. 21, 1948, the patient had changed completely in personality and exhibited no further emotional displays. Her mother was reassured and given counsel during weekly visits to the pediatrician. In an interview on Dec. 21, 1948, the parents said both they and the child had profited by the family physician's advice and were much happier. There had been no recurrence of F.'s temper outbursts.

Social Service Interview With Mother.—The mother was an exceedingly well-groomed and comely woman who was very conscious of her economic independence. She stated that she had been greatly upset two years previously by the death of her mother, upon whom she had been wholly dependent for love, security, and advice. Following the death of her father one year previously, she had begun to feel "terribly alone and insecure." She related that

oftentimes her nervous energy became so great that she would stand in the middle of the floor and scream and cry at the top of her lungs—all actions which the child, when frightened, would imitate.

Second Social Service Interview With Mother.—The mother felt that on her husband's return from service he had attempted to understand her nervousness and frigidity, but lately he had begun to stay out late and to ignore his wife except when criticizing her. He had arranged the new apartment so that he and his wife slept in twin beds. Recently he had become demanding, short-tempered, and had told his wife on several occasions that she "was spoiled and needed a good spanking like F." In the past two months he had retaliated, whenever the patient threw a tantrum in his presence, with a severe spanking. When annoyed by the child, he disciplined her by sending her to bed without supper or shutting her in a darkened room, advising her to "cry all she wanted to."[15]

Disposition of Case.—A program of de-emphasis of the mother's home activity and an opportunity for her to study interior decoration, home planning, and engage in community activity was arranged. The child was provided with nursery facilities under supervision of a trained psychologist. The parents were referred to their family physician who was able to adjust the parents' emotional misunderstanding and their mismanagement of the child.

CASE 4.—This case presents a slightly different approach and is included to illustrate the advantages when therapy of the patient is conducted in a convalescent home. Such facilities usually place an increased economic demand upon the parents. However, where symptoms persist and where the etiology of the illness remains obscure, this type of therapy has proved most successful.[16]

J. C., a 13-year-old Italian youth, was admitted Aug. 25, 1948, with a chief complaint of nervousness and vomiting associated with weight loss during the three weeks prior to admission to the hospital.

Past Medical History.—The parents described a normal birth and developmental history for this boy. There was no history of acute or chronic diseases.

Present Illness.—On Aug. 14, 1948, the patient had been a camper at a summer cabin with a group of eight boys his own age under supervision of a YMCA leader. J. had been free of symptoms before he left home, but after two days at camp he was sent home because he complained of anorexia and nausea with postprandial vomiting.[17] The patient stated that food at the camp was greasy and seemed "to stick in his throat." He just couldn't swallow it and when he had eaten a small amount of this food he would gag and vomit. During the ten days preceding his admission to the hospital he moped about the house, refused to eat at all, and cried when anyone tried to question him about his illness. He had no dysphagia, hematemesis, or dysarthria. He had lost about ten pounds during the period of fasting.

Physical Examination.—The patient appeared pale and asthenic, but was not acutely ill. He answered questions in a low voice, was easily upset, and

refused to look directly at the examiner. The examination was negative except for the patient's obviously weakened condition. A thorough neurologic examination was normal.

Laboratory Examination.—X-rays of the chest, gall bladder and gastrointestinal tract disclosed normally functioning organs. Blood, urine, and serologic studies were normal. Gastric drainage showed normal concentrations of free and combined acid.

Social Service Interview With Parents.—The parents believed the home life of the patient was a happy one; his siblings were free of nervous habits. However, the patient was described as always having been sensitive, quick to cry when his feelings were injured, and retiring among his playmates. He found school work difficult but with effort managed to maintain a "C" average.

The mother stated that since his return from camp he had refused to eat even specially prepared dishes of which he was very fond. He had had violent nightmares during which he tossed and turned restlessly, occasionally waking himself by crying out in his sleep. He told his mother that he had been picked on at camp. The other boys had warned him of bad men who would dope his food and then carry him away while he slept. J. had been afraid to eat, and even at home had told his mother "he knew the bad men would find him."[18]

Course in the Hospital.—The patient refused to eat solid or semisolid foods during the first three days of his hospitalization. Mild sedation produced no improvement and he continued to manifest profound nausea at the sight or odor of all food. On the first day gastric studies were done and the patient was given gavage feedings for twenty-four hours to accustom the shrunken, fasting stomach to food. J. protested, but retained all of these feedings.[19]

With assurance that forced feedings would cease only after he had begun eating of his own accord, J. took his first oral semisolid feedings on the fourth hospital day. With firm but kindly nursing care he had developed tolerance for the full house diet by the eighth day. Although the patient was more cheerful now, mention of home or camp or visits from his family would cause him to become nauseated and vomit even at this stage of convalescence.[20] Nevertheless, he was homesick.

Neither the house staff nor the neurological or psychiatric consultants were able to establish rapport with the patient to learn firsthand the incidents that had produced such a deep-seated anxiety. Because of the obscurity of these causes, and because of the patient's slow improvement while in the hospital, he was transferred out of the city to the convalescent ward on Sept. 10, 1948. After two days of recurrence of nausea and vomiting, J. gradually resumed eating and later began to play with the other children in the ward. However, a month elapsed before the weekly visits of his family ceased to upset him. At the time of his discharge to his family the patient had gained twelve pounds and was free of depression.

Disposition of Case: The patient visited Child Guidance Clinic for an interview on Dec. 18, 1948. At this time the social worker in charge of his case noted that J. was apparently the normal happy child he had been before the experiences of his camping trip in July had frightened him.

CASE 5.—The last two cases are typical of those most responsive to treatment by the family physician.

H. G., a 4-year-old white female child, was admitted Sept. 26, 1948, with a chief complaint of faulty eating habits associated with weight loss, increasing during the past six months.

Past Medical History.—The child had been born and had developed normally; no history of previous infectious or chronic diseases was given.

Family History.—There was one sibling, aged 3 weeks, living and well. The father, a draftsman aged 30 years, manifested an allergy for many foods and exercised constant care in the choice of his diet. He was also very limited in his food likes. The mother, aged 28, a college graduate, had been very nervous and easily upset since the birth of the patient.

Present Illness.—Since infancy the patient had been a poor eater. Up until she was 12 months of age she had eaten well only with coaxing and bribing. However, during the six months prior to admission, the patient had mimicked her father's intolerance for many foods, including bread and milk. She had no regard for her mother's attempts at discipline and the mother stated "she simply hadn't the heart" to be stern with the child.

Since the mother's duties as dietician necessitated catering to the whims of both her husband and child, she had become very temperamental, for she disliked cooking. The father, for this reason, became aggravated and would fly into a rage when the mother would mention her difficulties in planning the daily menu. During such outbursts the parents would argue as to whose fault it was that the child was ever born, and even criticize one another's poor taste as reflected in the child's appearance and her dress. Such discussions visibly upset the child and the mother said that H. would leave the table and shut herself in her room to sulk and cry. Since these arguments occurred most frequently at mealtime, the mother "wondered why the child ever ate anything any more."

Physical Examination.—The child was well developed, well nourished, and intelligent. There were no abnormal physical findings.

Laboratory Examination.—X-rays of the chest and gastrointestinal tract, together with complete blood count, urinalysis, sedimentation rate, and tuberculin test, were essentially negative.

Course in the Hospital.—Within twenty-four hours after admission the child was eating hungrily all food on her hospital tray. She was alert, happy, and active in group play. However, visits by the parents would depress the patient and cause her to lose her appetite for a short time.

Disposition of the Case.—The patient was discharged to the care of her grandmother for a two-week vacation while the referring practitioner undertook management of the family emotional problems.[21]

CASE 6.—C. P., a 13½-year-old white girl, was admitted May 5, 1948. The chief complaint was pain in the left chest of thirty-six hours' duration.

Past Medical History.—This child had had an appendectomy at Children's Hospital on April 2, 1948. She had an uneventful convalescence and was apparently well until the present admission. Otherwise the past medical history was negative.

Family History.—The mother and two siblings were living and well. There was no history of epidemic or chronic disease in the family.

Present Illness.—Thirty-six hours prior to admission the patient had suffered a sudden shaking chill followed by sharp substernal pain which had persisted in the left anterior and lateral chest.[22] The child complained that this pain would increase when she took a deep breath. She had no cough or fever on admission, although the mother stated that, following a chill twenty-four hours before admission, the child felt "as hot as if she had a temperature of 104 to 105°." The patient had been treated at home with penicillin and sulfa by the family physician without relief of her pain.

Eight months prior to her admission this patient's father had died of a heart attack. The attack occurred after dinner in the family living room in the presence of the entire family. The patient, always a sensitive child, had been greatly upset. Since this time she had been nervous and had been sleeping poorly.

The present attack of substernal pain occurred following C.'s return from the funeral services held for her high school principal. The child had returned from the funeral apparently in a state of emotional shock and the attack of chest pain occurred in the living room of her home following dinner. The mother stated that C. had been accustomed to seek the school principal's advice in her personal problems ever since her father's death. Upon investigation it was learned that the patient was aware that the school principal had also died of a heart attack.[23]

Physical Examination.—The patient was asthenic and apprehensive; she appeared acutely ill with rapid, irregular respirations. In addition to the complaint of chest pain she stated that her abdomen ached. The child stared at the ceiling during the examination and was vague in her response to questions. Neurological examination disclosed a marked hyperreflexia of the extremities and a tenseness of the abdominal musculature.

Laboratory.—Electrocardiogram and x-ray of the chest together with blood and urine examinations were reported negative.

Course in the Hospital.—While asleep the patient was observed to breathe deeply and regularly. Treatment with mild sedation and bed rest brought prompt recovery from the attack. Her angina-like pain disappeared on the second day. With simple reassurance and kindness the child forgot her symptoms and seemed bright and alert at the time of discharge on the sixth hospital day.

SUMMARY

1. Physicians today are more cognizant of psychosomatic illness in childhood.

2. This is evident at Children's Hospital of Pittsburgh, where the incidence of functional disorders has doubled since 1941.

3. Six cases are presented to illustrate the several manifestations of psychosomatic disorders in pediatrics.

The author is indebted to Drs. W. W. Briant, C. D. Kuhns, and E. L. Piper of the staff of Children's Hospital for their kind permission to include several of the case histories. He wishes to thank Drs. E. R. McCluskey, Chief of Staff and Professor of Pediatrics, T. S. Danowski, Professor of Research Medicine, and Maud L. Menten, Chief Pathologist at Children's Hospital, for their encouragement and advice in the writing of this paper. The author also wishes to thank Drs. Samuel Gomory, H. M. Little, and F. L. Weniger for their consultant services on the neurological and psychiatric aspects of these cases. The technical assistance of Mrs. Lauretta Frye in assimilating the social service interviews was most appreciated.

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Comments on Current Literature

THE SURGICAL TREATMENT OF MITRAL STENOSIS

A RECENT issue of the *Journal of the American Medical Association* carries an excellent resumé by Dr. B. Noland Carter[1] of the remarkable present-day accomplishments in surgery of the heart and allied great vessels. In discussing cardiac surgery, Carter refers briefly to recent attempts at intracardiac surgery, especially those concerned in the correction of certain types of valvular disease. He emphasizes in conclusion that "it behooves the medical profession in their efforts to reduce the present ravages of heart disease to be aware of what can be accomplished by surgical treatment."

In the April, 1949, issue of *Diseases of the Chest* Dr. Charles P. Bailey[2] discusses the surgical treatment of mitral stenosis. This report is of considerable interest to the medical profession since stenosis of the mitral valve is a comparatively common lesion and a particularly crippling one. Dr. Bailey emphasizes the serious prognosis of mitral stenosis and expresses the belief that there are at least 1,000,000 cases of mitral stenosis in the United States at the present time, one quarter of which are suitable for surgery.

In considering the advisability of attempting surgical relief of mitral stenosis, Bailey points out that pulmonary vascular congestion due to damming-back of blood behind the stenotic valve produces great distention of the left auricle and hypertension of the entire pulmonary vascular bed. While certain operative procedures have been used to relieve the high pressure in the pulmonary veins and left auricle, Bailey contends that this is merely a palliative measure since reduction of pressure in the left auricle would tend to reduce the amount of blood available for the rest of the body. Although the pulmonary signs of mitral stenosis might be improved by such procedures, in his opinion the general condition of the patient might be worsened. He, therefore, advocates direct approach to the problem by correction of the mitral stenotic lesion, employing a procedure which he has called "mitral commissurotomy." He reviews the literature, particularly that reporting experimental work on animals, and points out that regurgitation is undesirable, and may, if the commissurotomy is not done properly, result in aggravation of symptoms.

On the basis of autopsy studies of stenotic mitral valves, Bailey emphasizes that the "placque of thickened fibrotic tissue is surrounded by a margin of fairly normal valve tissue," and suggests that in an effort to correct the stenosis the stenotic valve may be cut in two by two incisions at the commissures of the valve opening. These incisions should be extended well into the normal valve tissue. If the chordae tendinae remain intact, such an operative result would allow the valve to act more efficiently, and would reduce the tendency to increasing regurgitation. Experience with five patients is reviewed in detail. Four of the five patients died, one apparently as a result of faulty fluid administration. The fifth, however, a 24-year-old white housewife, withstood the procedure very well and seemed greatly benefited by the operation. Seven and one-half months after surgery, the patient is able to do all her own housework, and her ballistocardiographic studies revealed marked improvement in cardiac output on exercise. Physical examination of the heart showed disappearance of the thrill and striking diminution of cardiac murmurs. An added note, dated Feb. 1, 1949, summarizes briefly the results on five additional patients who underwent this operation. Of these two are doing very well.

The discussion of this paper* merits attention. Dr. Evarts Graham, who was one of the pioneers in surgical attempts to cut the mitral valve, expressed enthusiasm at seeing the beautiful result obtained in the patient presented at the meeting, but cautioned that final judgment must be postponed for a year at least, since these valves which are cut have a tendency to grow together again. He also expressed the desire that physicians exercise care in the selection of patients for operative intervention, that suitable candidates for surgery be provided who are in fairly good physical condition, at least, since intracardiac surgery would have a greater chance of successful outcome if the patients offered a better operative risk at the outset.

During the general discussion Dr. Gordon Murray of Toronto, Canada, referred briefly to his own remarkable results. He explained that his procedure consists in a removal of one cusp of the valve and in a substitution in its place of a new valve constructed from a section of the cephalic vein and a segment of the palmaris longus tendon. Dr. Murray relates that by this operative procedure a valve cusp is reconstructed which seems to work satisfactorily.

Dr. Horace G. Smithy of Charleston, S. C., described experiments in which he was able to demonstrate that a 2 per cent solution of procaine infiltrated into the myocardium prevents the arrhythmias which have been difficult to control during cardiac surgery involving incision of the myocardium. Dr. Graham pointed out that the use of procaine in this manner may be of inestimable value in all cardiac surgery.

With the rapid improvement in anesthesia and general technique in surgical procedures involving the heart and great vessels, it seems possible that even more remarkable surgical correction of damaged hearts will be accomplished. The conception that patients crippled with mitral stenosis might be helped by surgical intervention is very encouraging. In the field of pediatrics, where rheumatic fever and its crippling effects on the heart are prominent phases, the possibility of actual surgical relief when mitral stenosis occurs is of more than academic interest.

If good results are to be expected with this form of intracardiac surgery, patients must be selected with great care, preferably while they are still in reasonably good physical condition. Perhaps surgical correction of mitral stenosis should be advocated in patients of the younger age groups. In any event, decisions concerning such patients require careful consideration and the best available diagnostic help before cardiac surgery is contemplated.

RUSSELL J. BLATTNER.

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*Dr. Bailey's paper was presented at the Fourteenth Annual Meeting of the American College of Chest Physicians, Chicago, June 20, 1948.

News and Notes

On April 5 a luncheon was held at the New York Academy of Medicine in honor of Dr. Sidney V. Haas and his completion of fifty years of pediatric practice. A Book of Tribute containing letters from 160 physicians and medical associations was presented to Dr. Haas. Dr. Haas is professor of pediatrics at the New York Polyclinic Medical School and Hospital and pioneered in the use of banana diet in celiac disease and the use of atropine in the treatment of the hypertonic infant.

The **Second Pan American Congress of Pediatrics** will be held at Mexico City, Nov. 2, 3, 4, and 5, 1949, immediately following the Third National Congress on the three preceding days. Physicians who register become members of the congresses. Fee $15.00 (U.S.A.) and for members of family $8.00 for social activities. There will be a scientific exhibit and exhibits and films should be sent to the Organizing Committee at least a month before the Congress. Speakers at the plenary sessions are invited by the Committee. Members may present contributions (ten minutes) at the Sectional Sessions.

The program for the Pan American Congress is as follows:

Tuesday, Nov. 1, 9 P.M. Dinner given by the Mexican Society of Pediatrics.

Wednesday, Nov. 2. First Plenary Session.

9 A.M. "Acute Diarrheas in Infancy" Dr. Félix Hurtado (Cuba), Relator. Among the speakers will be Dr. Alexis Hartmann (U.S.A.), Dr. Frederick Tisdall (Canada), and Dr. Federico Gómez (Mexico).

11 A.M. "Hemolytic Syndromes of the Newborn." Among the speakers will be Dr. Louis K. Diamond (U.S.A.) and Dr. Juan P. Garrahan (Argentina).

3-6 P.M. Sectional meetings.

Thursday, Nov. 3. Second Plenary Session.

9 A.M. "Cóngenital Malformations of the Heart" Dr. Agustin Castellanos (Cuba), Relator. Among the speakers will be Dr. Rodolfo O. Kreutzer (Argentina), Dr. Antonio Prado Vértiz (Mexico), and Dr. Eugenio Tousaint (Mexico).

11 P.M. "B.C.G. Vaccination in America." Among the speakers will be Dr. S. R. Rosenthal (U.S.A.), Dr. José Bonaba (Uruguay), and Dr. Arlindo de Assîs (Brazil).

3-6 P.M. Sectional meetings.

Friday, Nov. 4. Third Plenary Session.

9 A.M. "Pediatric Surgery." Among the speakers will be Dr. Herbert Coe (U.S.A.), Dr. Willis J. Potts (U.S.A.), and Dr. Jesús Lozoya Solís (Mexico).

11 A.M. "Virus Diseases in Pediatrics." Among the speakers will be Dr. Joseph Stokes, Jr. (U.S.A.), Dr. John A. Toomey (U.S.A.), and Dr. Rustin McIntosh (U.S.A.)

3-6 P.M. Sectional meetings.

Saturday, Nov. 5. Fourth Plenary Session.

9 A.M. "Child Neuropsychiatry." Among the speakers will be Dr. Florencio Escardó (Argentina) and Dr. Jorge Muñoz Turnbull (Mexico).

11 A.M. "Pediatrics in the Field of Social Security." Among the speakers will be Dr. Manuel Salcedo (Peru), Dr. Leslie Nelles Silverthorne (Canada), and Dr. John P. Hubbard (U.S.A.).

1 P.M. Banquet.
4-7 P.M. Business and Closing Session.
9 P.M. Dancing.

Full details may be obtained from the Secretary of the Second Pan American Congress, Dr. Alejandro Aguirre, Hospital Infantil, Mexico City, Mexico.

Sixth International Congress of Pediatrics, Zurich, 1950.

1. It has been decided to hold the Congress during the last ten days of July, 1950. The actual Congress will last four to five days, July 24 to 28. It is proposed to hold two plenary sessions, each lasting one-half day, and a series of simultaneous group sessions. A plan for the group sessions has been drawn up, based on suggestions from all over the world.

Each group session will consist of prearranged lectures lasting from ten to thirty minutes, followed by open discussion in which no contribution may exceed five minutes. Proposals for important lectures not included in the program can only be accepted through the secretariats of the various national Pediatric Associations.

2. The manuscripts of lectures (without illustrations) must reach the Organizing Committee not later than April 1, 1950, to permit their being printed and issued to conference members in advance.

3. It is planned to hold a scientific exhibition lasting two weeks in a hall adjoining the Conference rooms to display the lecturers' curves, photographs, etc. The Organizing Committee will provide free of charge the exhibition space and cellotex sheets necessary to hang the curves. Showcases for diapositives, coloured photographs, etc., can only be provided if ordered and paid for well in advance. All those invited to lecture can display their material; other conference members must secure special permission from their national Pediatric Associations beforehand.

4. Those who wish to attend the Congress and those who plan to show an exhibit are requested to advise the Secretary of the Congress.

Dr. Martha Eliot, Associate Chief of the Children's Bureau, has resigned to become Assistant Director General of the United Nations World Health Organization. Dr. Eliot, who has been associated with the Bureau for twenty-five years, will go to Geneva on June 1. Dr. Leona Baumgartner, Assistant Commissioner of Health for New York City, has been appointed to the Children's Bureau to fill Dr. Eliot's place on a six months' leave of absence from her present position.

On April 5 the **Alumni Association of the Children's Hospital, Washington, D. C.,** had its first meeting. About eighty-five former and present members of the house staff were present. Dr. Joseph S. Wall was elected president of the Association, Dr. Edgar P. Copeland vice-president, and Dr. Archibald R. MacPherson, 1220 W Street, N.W., secretary-treasurer. The Association is desirous of getting in touch with all former members of the staff.

Book Reviews

Safeguarding Motherhood. Sol T. DeLee, M.D., Philadelphia, J. B. Lippincott Company, 135 pages. Price $2.00.

The nephew of Joseph B. DeLee brings the famous obstetrical name to the field of prenatal care. The author has carefully solved the difficult problem of covering the prenatal subjects adequately in a short presentation. The various phases of conception, development of pregnancy, labor, and the post-partum period are treated in a simple, concise manner. An excellently presented section of the book deals with "Mental Attitudes and Beliefs," and will aid greatly in dispelling the superstitions and "old wives tales," with which every pregnant woman is besieged. There is a proper emphasis upon a well-balanced but controlled diet and a controlled weight gain during pregnancy. Certainly the advice given in this chapter could be taken as well by many obstetricians as by their patients.

Discussion of the various common disorders and also the more serious complications is brief and may be criticized by the generality that a little knowledge is a dangerous thing. Perhaps patients are unnecessarily disturbed mentally by imagining many symptoms and we question the advisability of attempting to explain these complications. The glossary contains technical terms probably unfamiliar to the mother and greatly increases the patient's understanding of the subjects discussed. G. J. L. WULFF, JR.

Fetal and Neonatal Death. Edith L. Potter, M.D., and Fred L. Adair, M.D., Chicago, 1949, University of Chicago Press, 174 pages. Price $3.75.

A second revised edition of this well-known text published in 1939. The new edition not only brings the statistical portion up to a recent date, but there are many changes in the text in keeping with medical developments as the Rh factor. Like the first edition, the book is definitive in its field.

The Oculorotary Muscles. Richard A. Scobee, M.D., St. Louis, 1947, The C. V. Mosby Company, 359 pages.

Strabismus, A Clinical Handbook. George J. Epstein, M.D., Philadelphia, 1948, The Blakiston Company, 214 pages.

The Management of Binocular Imbalance. Emanuel Krimsky, M.D., Philadelphia, 1948, Lea & Febiger, 464 pages.

Neurology of the Ocular Muscles. David G. Cogan, M.D., Springfield, Ill., 1948, Charles C Thomas, 214 pages.

The appearance during the past year or so of these four books on the extraocular muscles is indicative of an accumulation of much new knowledge on this subject. The methods of examination have become much more detailed and accurate, resulting in exceedingly exact diagnoses. From a more expanded knowledge of visual physiology, especially in the fields of fusion and of suppression, a more accurate idea of the mechanism behind strabismus has developed. Finally, in the field of treatment there has been advance, not only in the surgical methods, but even more noteworthy in the rapidly advancing subject of orthoptic training.

All of these books are primarily for the ophthalmologist and are, therefore, quite technical in approach. The material and ideas of the authors differ in many aspects, but result in a satisfactory coverage of the subject. Although ophthalmologic in character, these books can give to the pediatrician an adequate idea of the fundamentals of this subject which is so necessary if the patient is to get the best final visual and cosmetic result.

All the material presented in these books gives emphasis to the modern concept of very early, complete, and energetic ophthalmic treatment in these cases. SANDERS.

Editor's Column

ACCIDENTS

THE increasing importance of accidents as a major cause of death in childhood has been referred to editorially in THE JOURNAL previously. We have a great deal to learn about accidents, and hence information as to the age distribution, place, cause and character of the accident and the like are important in any sound attempt to lower the accident rates. It is for this reason that we publish a three-month study of accidents occurring in children treated at St. Luke's Hospital in Bethlehem, Pa., a city of some 65,000 population. The period included three summer months, and a comparison with three winter months when many children are attending school would, in all probability, show many differences.

During this period 566 children under 18 years of age were treated at the hospital, or an average of over six each day. It is of interest that there were no fatalities, although eleven cases necessitated major surgical procedures. About one child in six, or an average of one a day, had to be admitted to the wards, where the patient remained on an average of between seven and eight days. Assuming the hospital cost was $10.00 a day, we have calculated that the total cost for hospital care amounted to $6,500 for the three months, to say nothing of the x-rays, dressings, penicillin, antitoxin, etc., for the outpatient cases. Thus we can estimate that it costs the hospitals, or someone, $30,000 or more a year to take care of the children accidently injured in Bethlehem. If we add to this the accident cases treated by private physicians the total cost would be much greater. We leave it to the reader to estimate the medical bill for children injured each year in the United States. It must be enormous. This aside from the many fatalities, and the permanent crippling of many children.

Several interesting facts are brought out in this study. One is the tendency for accidents to increase the latter part of the day. Another is the peak in the third year of life. The older practitioners will note the almost negligible number of accidents due to fireworks around the fourth of July. We recall when "the Fourth" strained the facilities of the receiving ward and hospital. Legislation banning firecrackers has largely wiped out this cause for accidents. How much more legislation can accomplish in further reducing the accident rate is problematical. We hazard the guess that in the future education as to the importance and causes of accidents will do more to lower the accident rate in childhood than legislation.

DR. ELIOT AND THE CHILDREN'S BUREAU

THE retirement of Dr. Martha Eliot from the Children's Bureau calls for more than a mere news item. Her appointment to the World Health Organization as Assistant Director General is a tribute to her ability and energy and to the sincerity of her work over many years to provide better health for women and children. Many physicians and the JOURNAL have not at times seen eye to eye with her as chief medical officer of the bureau, to which she has been attached for nearly a quarter of a century. There have been no disagreements as to ends or purposes, but rather honest differences of opinion as to the best means and ways to reach the goal. Despite these disagreements there has always been the greatest respect for Dr. Eliot as a physician and as an individual.

The differences of opinion have developed in large part from the feeling that the Children's Bureau has been active in promulgating a kind of social and political philosophy which is not involved in the primary purpose of the bureau of bringing about better maternal and child health, as this is fundamentally a technical problem of medicine and education. How much of this policy has stemmed from Dr. Eliot, and how much of it from the "higher ups" is a question we are not in a position to answer, but her position as medical chief has, of necessity, involved her representing bureau policies to the medical profession. For some reason or other government bureaus of all kinds (as recently highlighted by the Hoover reports) tend gradually to overemphasize the importance of the bureau, to look upon the bureau as an end in itself rather than a means to an end, to assume the function of policy-making rather than of carrying out policy as formulated by the people. This does not mean that the Children's Bureau has not made sound contributions to the health of American children, and this we attribute in no small part to Dr. Eliot's influence and ability. We all wish her success in her new position.

B. S. V.

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